

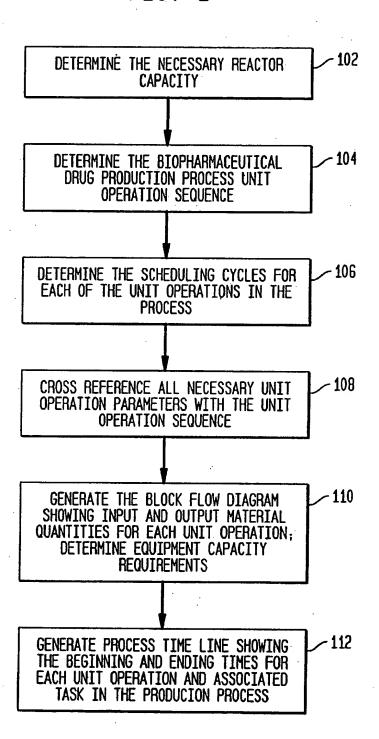
Replacement Sheet Sheet 1 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998 Dkt No.: 1606.0020004; Group Unit: 2128 Inventor: Peter G. BROWN; Tel. No.: 202-371-2600 For: Method for Scheduling Solution Preparation in

Biopharmaceutical Batch Process Manufacturing

(As Amended)

# FIG. 1

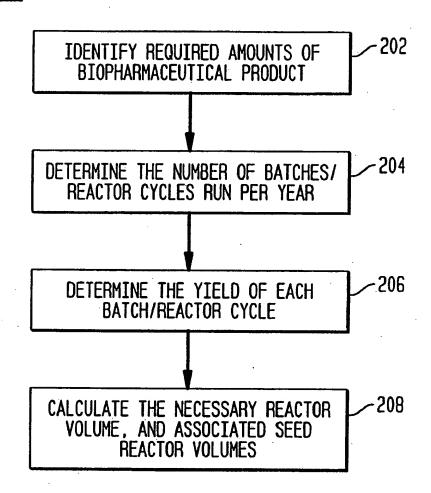


Replacement Sheet

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(1s. Amandod) (As Amended)

FIG. 2

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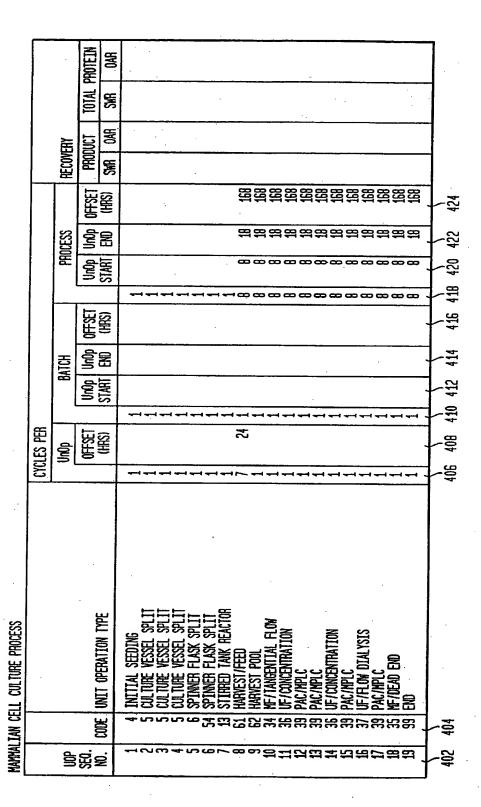
Replacement Sheet
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MICROBIAL FERNENTATION PROCESS

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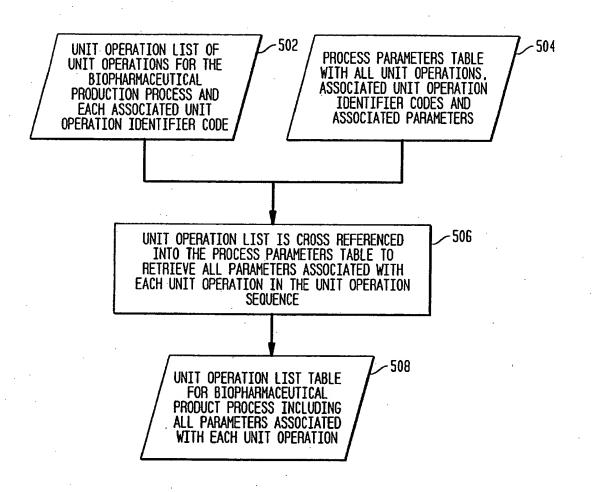


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## FIG. 5



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# FIG. 6A

	•	
UNIT OPERATION ID CODE	UNIT OPERATION TYPE	PARANETERS
í	INOCULUM PREP	* OF FLASKS, VOLUME OF FLASKS, TEMPERATURE, AGITATION, DURATION, FINAL OC
2	FLASK GROWTH	SCALE UP RATIO, MEDIA VOLUME, TEMPERATURE, AGITATION, DURATION, FINAL OD
3	FERMENTATION SEED	SCALE UP RATIO, FERMENTOR WORKING YOLUNE, ANTIFOAM, BASE ACID, GROW TEMPERATURE, AGITATION, SPARSE RATE, BACK PRESSURE, IOTAL DURATION
4	FERMENTATION PRODUCTION	SCALE UP RATIO, GERMENTOR WORKING VOLUME, ANTIFOAM A, ANTIFOAM B, BASE, ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL OURATION, FINAL OK, DRY CELL MASS, PRODUCT CONCENTRATION, CIP, SIP
5	HEAT EXCHANGE	PROCESS INITIAL & FINAL TEMP. UTILITY INITIAL & FINAL TEMP. PROCESS SPECIFIC HEAT; Design type, step recovery of product, step recovery of 1.p., temperature Regulation, c1p., s1p
6	BATCH CENTRIFUGATION	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE
7	RESOLUBLIZATION RESUSPENSION	REAGENT/PRODUCT RATIO. TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF THE PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
8	CELL DISPUPTION HIGH PRESS. HONHOGENIZATION	PRODUCT TERPPERATURE, UNILLITY TEMPERATURE, VOID VOLUME, NUMBER OF PASSES, PRESSURE, FLOW RATE, TEMPERATURE TROPEASE, WASH, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF J.P., TEMPERATURE REGULATION, CIP
9	DILUTE WITH SURFACTANT	REAGENT PRODUCT RATIO, TITRATION SOLUTION, DILUTION TIME, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP. STP
10	BATCH CENTRIFUGATION PRECIPITATE HARVEST	SYSTEM VOID VOLUME, RCF., TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
11	resuspend with Chaotrope	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME. STEP RECOVERY OF PRODUCT, STEP RECOVERY TO TP, TEMPERATURE REGULATION, CIP, SIP
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# FIG. 6B

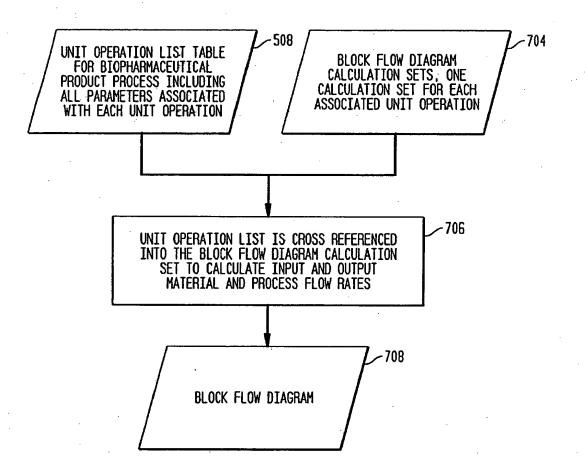
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SOLUTION TYPE	TASKS	TASK DURATION
S-101	SETUP, PREINCUBATION, Incubation, Clean UP	3, 3, 23, .3, HRS
S-101	SETUP, PREINCUBATION, Incubation, Clean UP	1, 1, 23, .3, HRS
S-101, 102, 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, HARYEST, CIP, SIP, CLEAN UP	1, 1, 21, .5, 1, 1, 3 HRS
S-101, 102 103, 104, 105	SETUP, PREINCURATION, Fernentation, CIP, SIP, Clean UP	•
	SETUP, TRANSFER, CIP, SIP, CLEAN UP	•
S-106	SETUP, CENTRIFUCATION, WASH, CIP, SIP, CLEANUP	•
S-107	SETUP, DILUTION, AGITATE, CIP. SIP, CLEAN UP	•
S-107	SETUP, LYSIS, CIP, SIP, CLEAN UP	. •
S- <b>1</b> 08	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	
S-108	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEAN UP	•
S-109	SETUP, FLUSH, PRIME, Concentration, dilution, Wash, Flush, Store, CIP, SIP, Cleanup	•
		•

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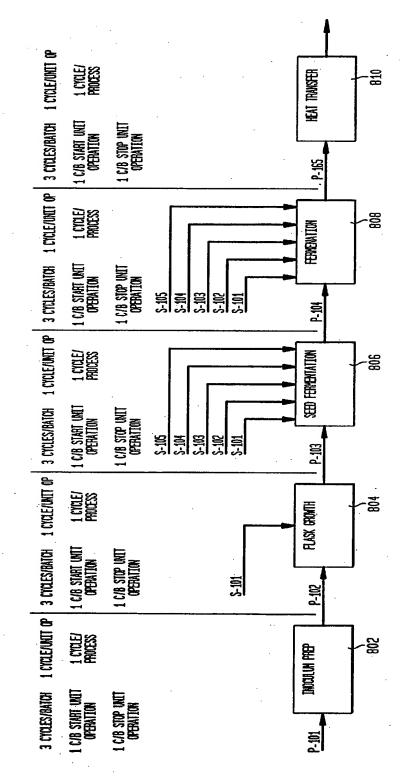
(As Amended)

FIG. 7



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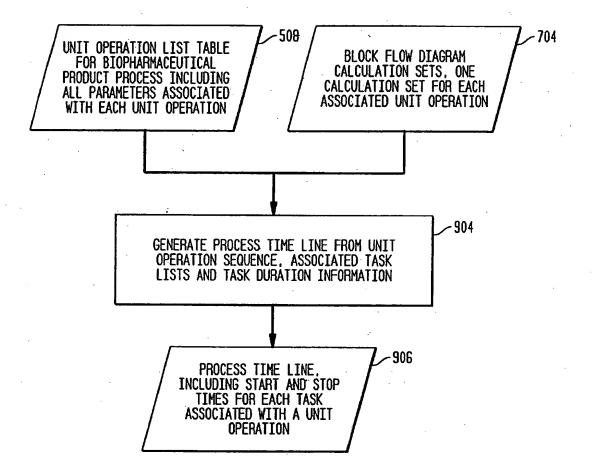
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FIG. 9



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# FIG. 10

### SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING

KICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)

	!	FIRST PRO	OCESS CYCLE SE	CON	) Process	S CYCLE
OU	RATION	WEEK	DAY	WEE	EK (	DAY
NOTE: NONE OF THE UNIT OPERATIONS IN THIS PR (SEE UNIT OPERATION 8 IN THE MANMALIAN CELL (	OCESS HAVE NORE THAT 1 C' Culture process for an ei	YCLE PER Xanple of	UNIT OPERATION • Multiple cycles per	UN)	IT OPERA	(ION)
UNIT OPERATIONS 1-6 UNDERGO THREE REPETATIVE THIS TRANSLATES TO THREE RUNS ON A FERMENTOR ASSOCIATED WITH EACH FERMENTOR RUN (UNIT OP 4 1/3 FERMENTATION CYCLES PER RATCH	WITH CAME HANDERT JUNITY	AN E P P	<sup>ነ</sup>	MAI 1	IN AT IN	IIT OP 7
ASSOCIATED WITH EACH FERMENTOR RUN (UNIT OP 4  1/3 FERMENTATION CYCLES PER BATCH  1 INOCULUM PREP  2 FLASK GROWTH  3 SEED FERMENTATION  4 PRODUCTION FERMENTATION  5 HEAT EXCHANGE  6 CENTRIFUGATION  2/3 FERMENTATION CYCLES PER BATCH  1 INOCULUM PREP  2 FLASK GROWTH  3 SEED FERMENTATION  4 PRODUCTION FERMENTATION  5 HEAT EXCHANGE  6 CENTRIFUGATION  3 SEED FERMENTATION  5 HEAT EXCHANGE  6 CENTRIFUGATION  3/3 FERMENTATION CYCLES PER BATCH  1 INOCULUM PREP  2 FLASK GROWTH  3 SEED FERMENTATION  3 SEED FERMENTATION  4 PRODUCTION FERMENTATION  5 HEAT EXCHANGE  6 CENTRIFUGATION  4 PRODUCTION FERMENTATION  5 HEAT EXCHANGE  6 CENTRIFUGATION  1 INOCULUM PREP  2 FLASK GROWTH  3 SEED FERMENTATION  4 PRODUCTION FERMENTATION  5 HEAT EXCHANGE  6 CENTRIFUGATION  1 INDICATED THE HARVESTS FROM THE	24 HRS 24 HRS 24 HRS 24 HRS 1 HR 1 HR	1 FRI 2 SAT 2 SUN 2 MON 2 TUE 2 TUE	- SAT - SUN I - MOH I - TUE		FRI - S SAT - S SUN - H HON - T TUE	iat Iun Ion Ue
1 INOCULUN PREP 2 2 FLASK GROWTH 2 3 SEED FERMENTAION 2 4 PRODUCTION FERMENTATION 2 5 HEAT EXCHANGE 1 6 CENTRIPUGATION 1	24 HRS 24 HRS 24 HRS 24 HRS 1 HR 1 HR	2 SUN 2 KON 2 TUE 2 WED 2 THU 2 THU	- MON   - TUE   - VED   - THU	3333333	SUN - M MON - T TUE - W WED - T THU	ION VE TED HV
J/J. PERPENTATION CTULES PER BATCH  1 INOCULUM PREP  2 FLASK GROWTH  3 SEED FERMENTATION  4 PRODUCTION FERMENTATION  5 HEAT EXCHANGE  6 CENTRIPUGATION  1	44 HRS 44 HRS 44 HRS 44 HRS 4 HRS 1 HR	2 TUE 2 WED 2 THU 2 FRI 2 SAT 2 SAT	- WED - Thu - Fri - Sat	33333	TUE - W WED - T THU - F FRI - S SAT SAT	ED HU RI AT
UNIT OPERATION 7 POOLS THE HARVESTS FROM THE 7 POOL HARVESTS 3 INIT OPERATIONS 8-9 UNDERSO THREE REPETATIVE THIS TRANSLATES TO THREE CONSECUTIVE PASSES TO SUMIT OP 8 & 10) AT THE INLET AND THE OUTLET OF 1/3 DISRUPTION CYCLES PER BATCH	THREE FERHENTATION CYCLE I HR Cycles per batch as set Hrough cell disruptor (u Of the cell disruptor	S ABOVE 3 MON BEFORE CO NIT OP 93	ONTINUING WITH UNIT ( ) WITH ITS ASSOCIATED	OPER OPER	MON ATION 11 AT EXCHA	NGERS
8 HEAT EXCHANGE 9 CELL DISRUPTION 10 HEAT EXCHANGE 0 2/3 DISRUPTION CYCLES PER BATCH 8 HEAT EXCHANGE	.5 HR	3 HON		4	HON	
9 CELL DISRUPTION 10 HEAT EXCHANGE 0 3/3 DISRUPTION CYCLES PER BATCH 8 HEAT EXCHANGE 9 CELL DISRUPTION	.5 IR	3 MON		4	MON	
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# FIG. 11

## SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING

HICROBIAL FERNENTATION PROCESS	S (SEE UNIT OPERATION LIST)		*
		FIRST PROCESS CYCLE	SECOND PROCESS CYCLE
	DURATION	WEEK DAY	WEEK DAY
THIS TRANSLATES TO TWO CYCLES SURFACTANT AND RECONCENTRATING 1/2 PRODUCT WASHING CYCL	G OF RESUSPENDING THE CELL TYSAT IG THE INSOLUBLE PRODUCT TO A PA ES PER BATCH	SET BEFORE CONTINUING WITH UNIT E FROM THE CELL DISRUPTOR IN A I STE BY CENTRIFUGATION	<b>0° 13</b> TILO
11 RESUSPENSI 12 Centrifuga 2/3 product Vashing Cycl		3 MON 3 MON	4 HON 4 HON
11 RESUSPENSI 12 CENTRIFUGA	ON 0.5 HR	3 KON 3 KON H TO THE END OF THE DOGGES	4 KON 4 KON
13 RESUSPENSI 14 BUFFER EXC 15 FILTRATION 16 LIQUID CHR 17 LIQUID CHR 18 BUFFER EXC 19 LIQUID CHR 20 BUFFER EXC	ON 0.5 HR HANGE 2 HR 2 HR OMATOGRAPHY 16 HRS OMATOGRAPHY 4 HRS HANGE 2 HRS OMATOGRAPHY 2 HRS HANGE 2 HRS OMATOGRAPHY 2 HRS OMATOGRAPHY 2 HRS OMATOGRAPHY 2 HRS	3 KON 3 KON 3 KON 3 KON 3 KON 5 KON 7 TUE	4 MON 4 MON 4 MON 4 MON - TUE 4 TUE 4 TUE 4 WED 4 WED 4 WED 4 WED

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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Replacement Sheet
Sheet 16 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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Replacement Sheet
Sheet 17 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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Replacement Sheet
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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Replacement Sheet
Sheet 19 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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Replacement Sheet
Sheet 20 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

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Replacement Sheet
Sheet 21 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
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Replacement Sheet
Sheet 22 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing,
(As Amended)

### CANT. CBRT/AULINS  #### CANT. CBRT/AULINS  #### CANT. CBRT/AULINS  #### CANT. CBRT/AULINS  #### CANT. CBRT/AULINS  #### CANT. CBRT/AULINS  #### CANT. CBRT/A	-	8	3. 多	T	T	经	<del>2</del>	T	T	\$2	88		т	Т
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Replacement Sheet
Sheet 23 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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Replacement Sheet
Sheet 24 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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Replacement Sheet
Sheet 25 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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Replacement Sheet Sheet 26 of 167 Appl. No.: 09/100,088; Filed: June 19, 1998

Dkt No.: 1606.0020004; Group Unit: 2128 Inventor: Peter G. BROWN; Tel. No.: 202-371-2600 For: Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing

Replacement Sheet
Sheet 27 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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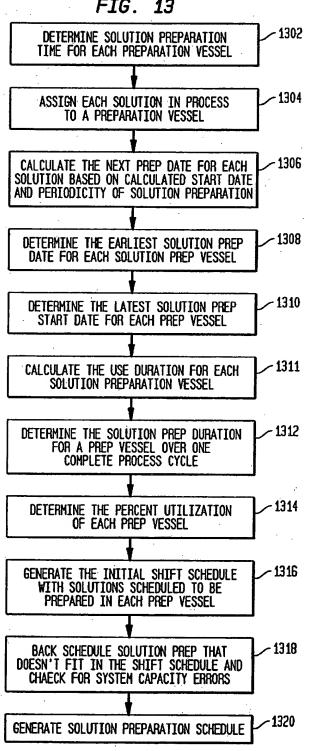
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Replacement Sheet Sheet 28 of 167 Appl. No.: 09/100,088; Filed: June 19, 1998 Dkt No.: 1606.0020004; Group Unit: 2128

Inventor: Peter G. BROWN; Tel. No.: 202-371-2600 For: Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing

(As Amended)

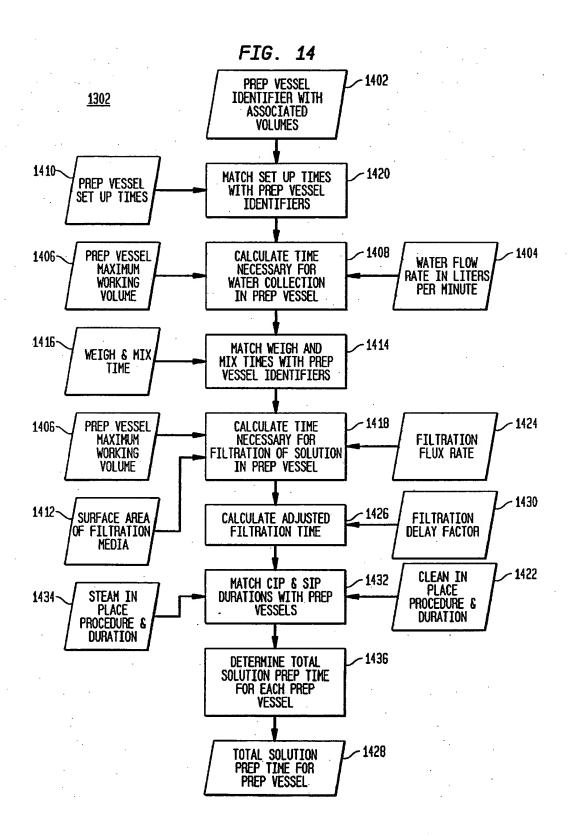
### FIG. 13



#### Replacement Sheet Sheet 29 of 167

Appl. No.: 09/100,088; Filed: June 19, 1998 Dkt No.: 1606.0020004; Group Unit: 2128 Inventor: Peter G. BROWN; Tel. No.: 202-371-2600 For: Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing

(As Amended)



Replacement Sheet
Sheet 30 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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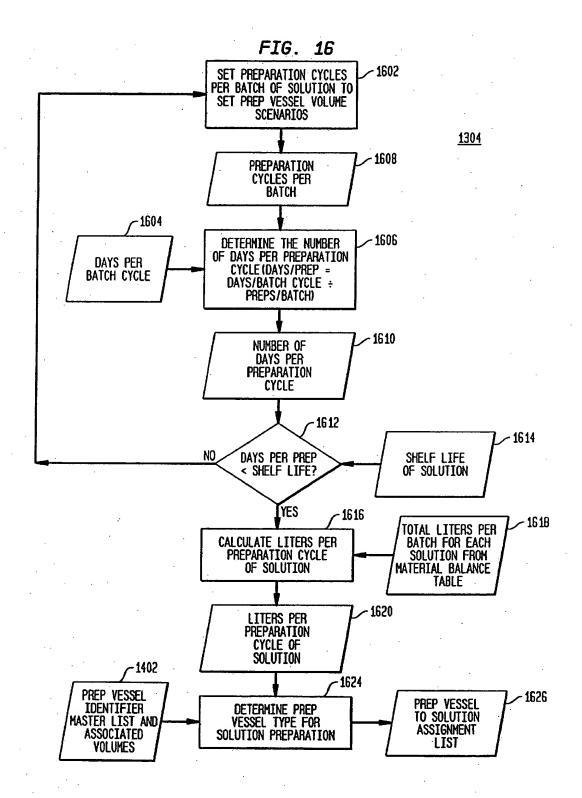
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ULTE	R2	5:4422\$\$\$\$\$\$ \$388888\$	1412
יאבונאי	AN N	44888888888	1410
ÓLLECT.	NIW.	ままろまろらむられ犯訟。	1502
WATER COLLECT	LPM.	. 2222222	1404
	SET UP MIN.	00000000000000000000000000000000000000	1410
BATCH TANK BATCH TANK	MAX. Lw	1,500 20 100 100 250 500 500 500 500 500	1406
	HIN. LW	0.5 1 10 20 50 50 500 1500	1402
	NO.	110000000000000000000000000000000000000	
	MIN.	0.5 10 10 20 50 500 500 1500	
	<u>\$</u>	101 102 103 103 103 110 110 110 110 110 110 110	

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(As Amended)



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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 17 Solution Prep Campaign Format

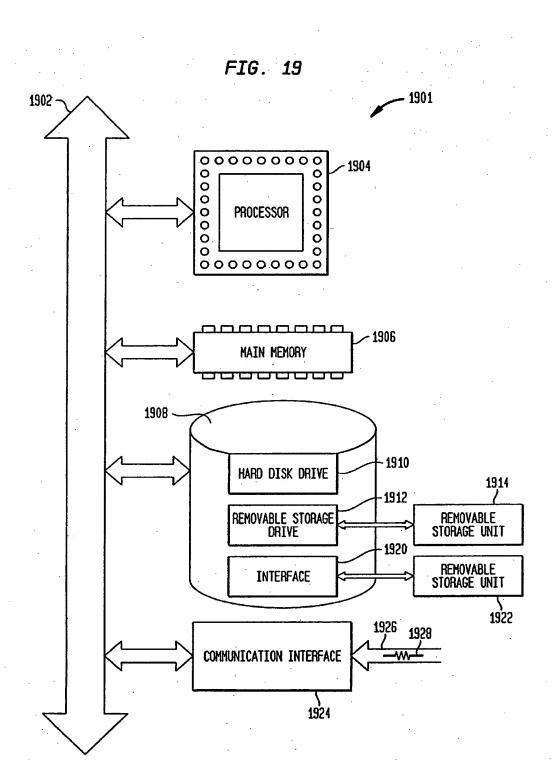
101	88	107	F	<u>-</u>
123	೭೫	108	T	~5
記	98		7	; ۱
5	48	104	ļ	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
<b>E</b>	24		ļ	47.49
102	44.¢	201	Ļ	1740
191	0.5		F	4700
	Shelf Check	888888888888888888		1000
	Shelf Days			10.01
	Days/ Prep			- <del>1</del> 040
	Days/ Bat.Cy.			<b>-</b>
les	Liters/ Prep	1,565.50 1,555.90 1,5		-5 <u>5</u>
Prep Cyc	Preps/ Batch		7	~62
Format Solution Prep Cycles	Liters/ Batch	1, 665.5 1, 155.5 1,	}	( ) 10,10
ormat	BIA	00000000000000000	П	
rep F	. 68	*****	П	
Soln.Prep	Ş	0000000000000000	П	
	웃	·	H	
Storage Cond.	40		H	
Stora	⊭	*****	П	
	E C		7	1704
			$\dashv$	

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 18		Tank Fill				
		Tank Assignment Solution Prep Schedule	Prep.	च थ च च च च च च च च च च च च च च च च <del>च च च</del>		
			Next Prep	888888888888888888888888		06/14/96
			Final Start	05/23/36 05/31/36 05/31/36 05/31/36 05/07/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36		05/29/96 Min
			Float Days	0000000000000000000		ž.
			Init. Start	05/29/36 05/31/36 05/31/36 05/31/36 05/31/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36 06/07/36		
	ormat		Hold Days	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	П	
	ampaign Fi		Avail. By	05/31/36 06/04/36 06/04/36 06/04/36 06/04/36 06/11/36 06/11/36 06/11/36 06/11/36 06/11/36 06/11/36 06/11/36		
Ī	rep C		Back Days	स्त्रन्य संस्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स्त्र स		
363)	Solution P		Required By	06/03/96 06/03/96 06/05/96 06/05/96 06/11/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96 06/12/96		06/03/96 06/12/96 0
			Final Assign.	1994419899999999999999999999		Min Sat Sun
			Initial Assign.	199444888698118888888		
	9707	109. 110 111	3000	# #	7	1728
			500 1500	01 01	7	1726
			283	103	}	1724
	l	108	単級	108 108 108 108 108	1	1722
			SE P	\$\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\		
*			ľ	12月4567番号地址沿街社投場日間227		•

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

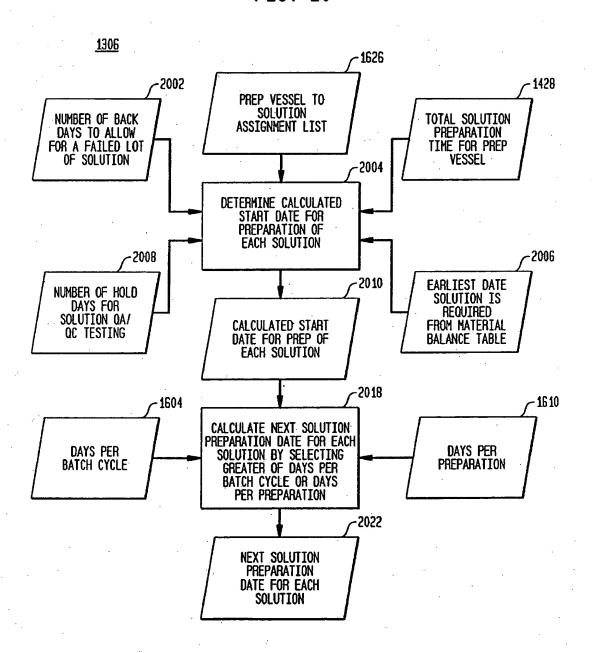


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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tcl. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing

(As Amended)

FIG. 20



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For: Method for Scheduling Solution Preparation in

Biopharmaceutical Batch Process Manufacturing

(As Amended)

FIG. 21A 2102

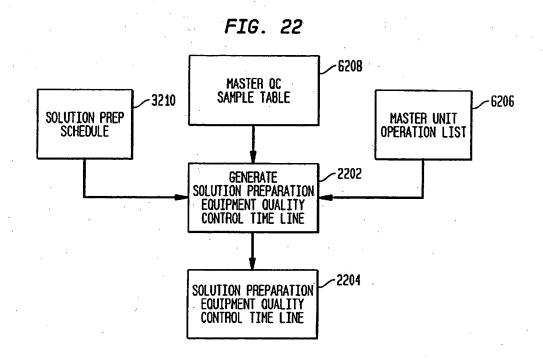
```
Category/Assay
      Environmental
 1
2
3
           Temperature
Humidity
            Particle Count
 5
     Analytical
Visual
 6
 8
                  Certificate of Analysis
                  Appearance
10
            Chemical
11
                  Solubility
pH
Osmolality
                  Water Content(by Karl Fischer)
Key Element Analysis(by ICP Atomic Adsorption Spectroscopy)
                  GC/Mass Spec
           Biochemical
                  DNA
                        DNA Fluorochrome Stain
                 Protein
                        Hemoglobin
                        Electrophoretic Profiles by SDS-PAGE
                        A280
                        Bradford Assay
                        Amino Acid Analysis by HPLC
                 Endotoxin
                        Gel Clot LAL
           Immunological
ELISA
                  Western Blots
           Activity
                 Chromagenic Substrate Assays
    In Vitro Biological
Microbilogical
           Mycoplasma(Barile Method)
Bacteriophage(Screened)
           Cell Passage Test
           Adventitious viral Agents
                 CPE
BVD
P13
                 IBR
           Virus Neutralization Titers(9CFR)
45
46
47
                 BVD
                 P13
                 IBR
           Tritiated Thymidine Uptake in Mouse Cells
General Safety Test(Guinea Pigs)
48
49
50
```

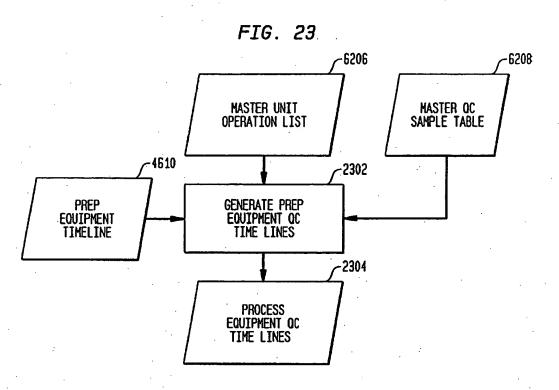
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaccutical Batch Process Manufacturing
(As Amended)

	2104		FIG. 2	1B 2106	
_	Code	Man Hour Set Up	Per Sample	Clean Up	Disp. Material
	E-1 E-2 E-3	0.5 0.5 0.5	0.1 0.1 0.2	0.5 0.5 0.5	
$\rangle$	AV-1 AV-2	0.25 0.25	0.2 0.05	0.5 0.25	
$\langle$	AC-1 AC-2 AC-3 AC-4 AC-5 AC-6	0.5 0.25 0.25 0.5 1	0.1 0.05 0.1 0.2 0.25 0.25	0.5 0.25 0.25 0.5 1	
	AB-1	0.5	0.1	0.5	
	AB-2 AB-3 AB-4 AB-5 AB-6 AB-7	0.5 0.25 0.5 1 0.5	0.1 0.2 0.1 0.1 0.25 0.1	0.5 1 0.25 0.5 1 0.5	
	AI-1 AI-2	1 1.5	0.1 0.2	1 1.5	
	AA-1	1	0.1	1	
	VB-1 VB-2 VB-3 VB-4 VB-5 VB-6 VB-7 VB-8	0.5 0.5 0.5 1 2 2 2 2	0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2	0.5 0.5 0.5 1 1 1 1	
	VB-9 VB-10 VB-11 VB-12 VB-13	2 2 2 1	0.2 0.2 0.2 0.2 0.2	1 1 1 1 1	

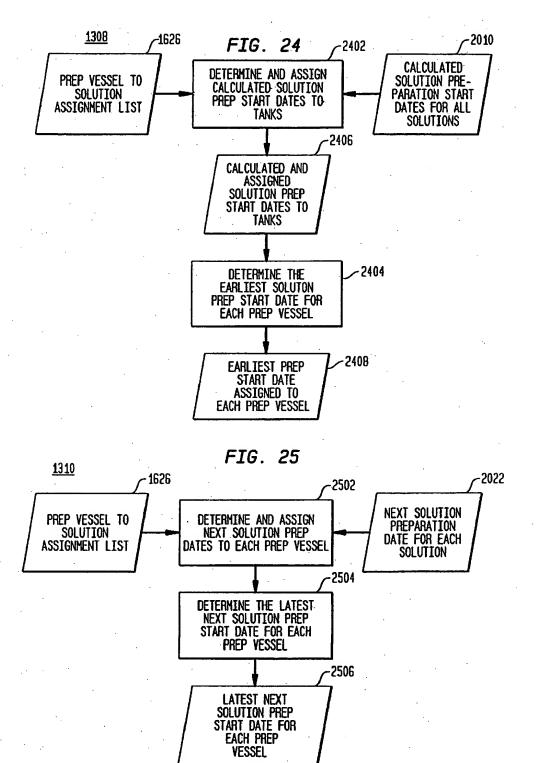
Replacement Sheet Sheet 38 of 167 Sheet 38 of 167

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)





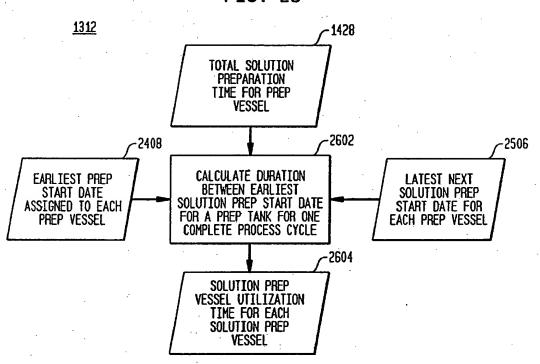
Replacement Sheet
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600

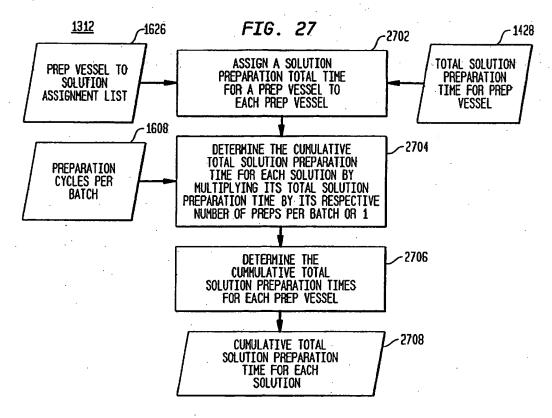
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing

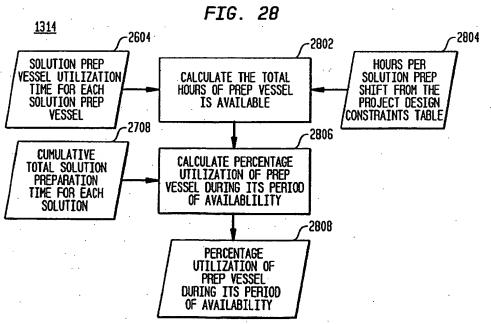
FIG. 26



Replacement Sheet

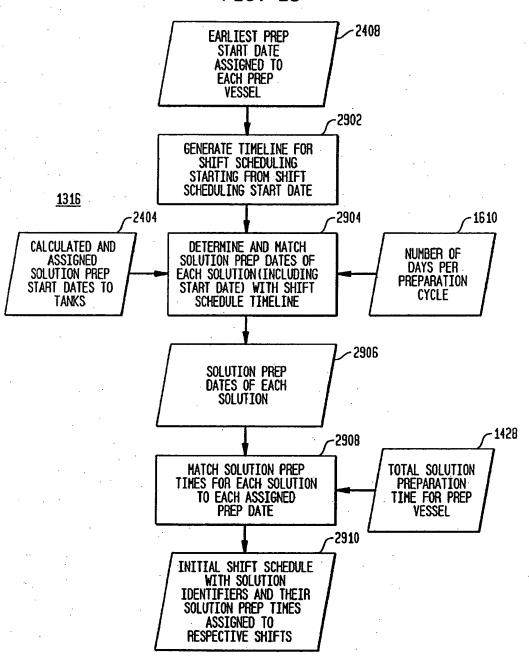
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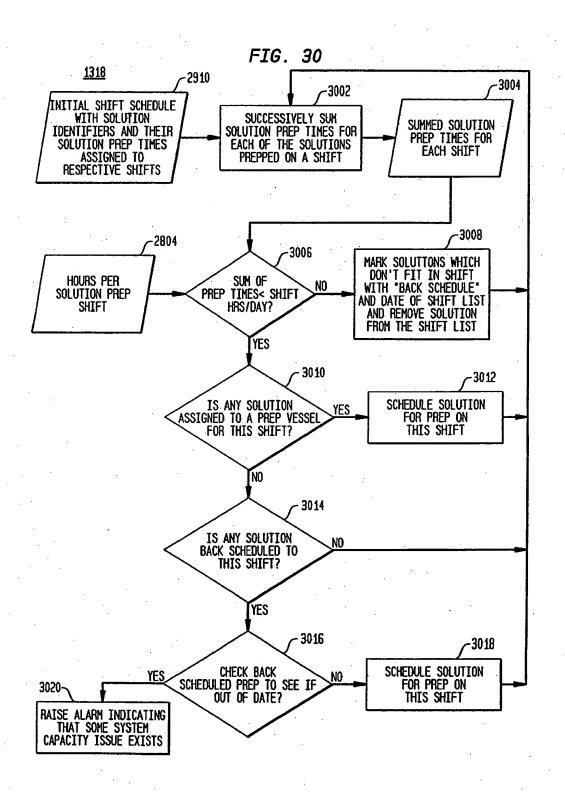
Replacement Sheet
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

## FIG. 31A

		2804									
		( 8	Hrs/Day	59		60		61		62	$\equiv 7$
Tank 10	1Usage	3.5 (	06/13/96 04/05/96	06/03/	96	06/04/	96	06/05/	96	06/06/	96
Soin.		Period	Start	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.
S-0101 S-0102 S-0103 S-0104 S-0105 S-0106 S-0107 S-0109 S-0111 S-0112 S-0113 S-0114 S-0115 S-0116 S-0117 S-0118 S-0119 S-0120 S-0121 S-0122	13.2 1.7 8.3 8.3 22.2	56 7 7 7	02/14/96 05/22/96 05/22/96 05/22/96 05/29/96	05/29/96 05/29/96 05/29/96		04/10/96 05/29/96 05/29/96 05/29/96 05/29/96		06/05/96 06/05/96 06/05/96 06/05/96	3.55 3.5 3.5	06/05/96 06/05/96 06/05/96 06/05/96 06/05/96	
					0		0		21		0
3102		1610		2906							

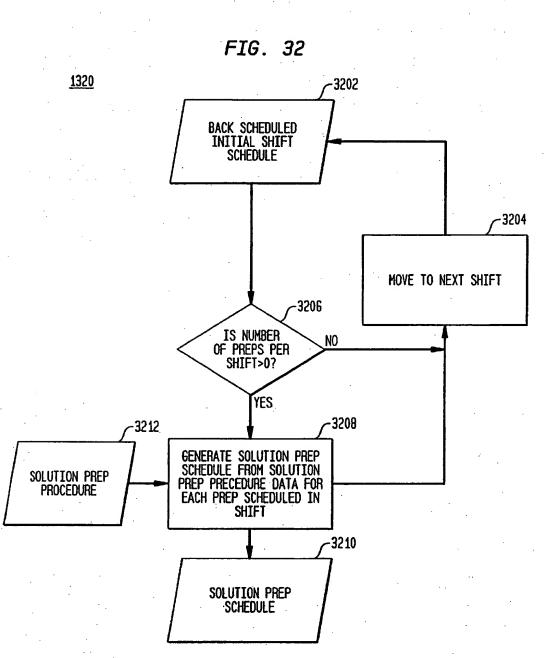
Replacement Sheet
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

# FIG. 31B

1	63		64		65		66		67		68	
(	06/07/	96	06/08/96		06/09/	96	06/10/	96	06/11/	96	06/12/	96
1	/ Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.
(	06/05/96 06/05/96 06/05/96 06/05/96		06/05/96 06/05/96 06/05/96 06/05/96		06/05/96 06/05/96 06/05/96 06/05/96		06/05/96 06/05/96 06/05/96 06/05/96		06/05/96 06/05/96 06/05/96 06/05/96		06/05/96 06/12/96 06/12/96 06/12/96	3.5 3.5 3.5
(	06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
\\\												
1	06/05/96	0	06/05/96	0	06/05/96	0	06/05/96	0	06/05/96	0	06/12/96	3.5 17.5

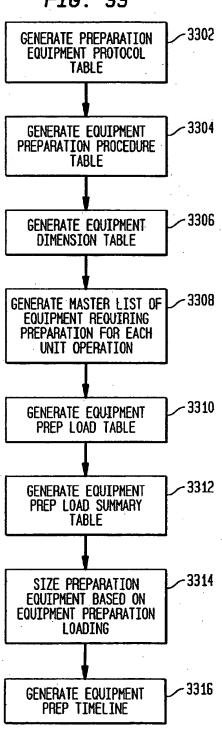
Replacement Sheet
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)



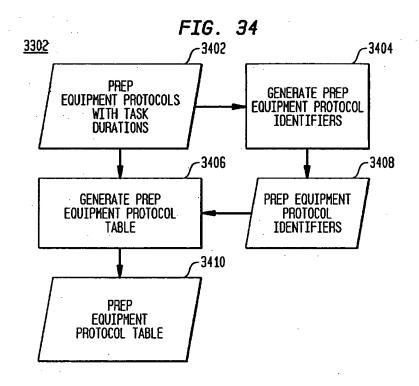
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Appl. No.: 09/100,088; Filed: June 19, 1998
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

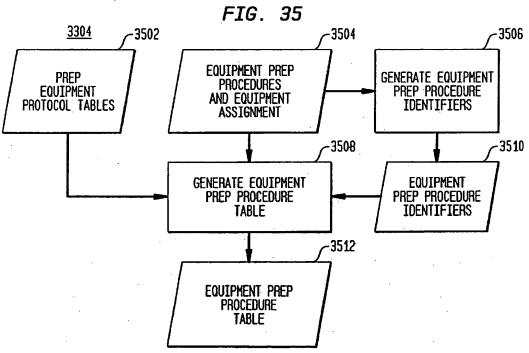




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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

(As Amended)

ನನನನನ

일을 <del>~~~~</del> でごろうごろ POST WASH PREP EQUIPMENT PROTOCOL-BENCH SINK 00000 GM/CF FIG. 36A S Alconox S Alconox S Alconox S Alconox PRE WASH RINSE NPHW NPCW <u>~~~~</u> MINUTES/CYCLE NUNNIN CYCLE

TOTAL

			<u> </u>
		FINAL	2222
		POST WASH RINSE NPHW NPCW	ನನನನ
ATION		POST WAS	2222
-WASH STA		HJ/W9	9000
PREP EQUIPMENT PROTOCOL-WASH STATION		NT WASH REAGENT	Alconox Alconox Alconox Alconox Alconox
OUIPMENT		DETERGENT MINUTES   P	സസസസ
PREP E		PRE WASH RINSE NPHW NPCW	22222
	MINUTES/CYCLE	PRE WAS	20000
	MINUT	LOAD	സസസസ
3408	_	ROTOCOL	**************************************

**#####** 

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(As Amended)

3408 PREP EQUIPMENT PROTOCOL-GLASSWARE WASHER  CYCLE  CYCLE  CYCLE  LOAD  NPHW NPCW MINUTES REAGENT WASH  1 GW-1  2 GW-2  1 GW-1  1 GW-1  1 GW-1  1 GW-1  1 GW-1  1 GW-1  2 GW-2  1 GW-2  1 GW-2  1 GW-1  2 GW-2  1 GW-1  2 GW-2  1 GW-1  1 GW-1  2 GW-2  1 GW-1  2 GW-2  1 GW-1  2 GW-2  1 GW-1  1 GW					T0TA	
### PREP EQUIPMENT PROTOCOL-GLASSWARE WASHER  ###################################					UNLOAD	99999
PREP EQUIPMENT PROTOCOL-GLASS  MINUTES/CYCLE  LOAD NPHW NPCW MINUTES REAGENT Gm/CF  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 5 5 Alconox 0.5  15 2 5 5 Alconox 0.5				FINAL	RINSE	2222
PREP EQUIPMENT PROTOCOL-GLASS  MINUTES/CYCLE  LOAD NPHW NPCW MINUTES REAGENT Gm/CF  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 5 5 Alconox 0.5  15 2 5 5 Alconox 0.5	•	监	,	SH RINSE	MDGN	222
PREP EQUIPMENT PROTOCOL-GLASS  MINUTES/CYCLE  LOAD NPHW NPCW MINUTES REAGENT Gm/CF  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 2 5 Alconox 0.5  15 2 5 5 Alconox 0.5  15 2 5 5 Alconox 0.5		WARE WASI		POST WAS	WPHW	2222
11.E MINUTES/CYCLE NINUTES/CYCLE NPHW NP NP NP NP NP NP NP NP NP NP NP NP NP	<i>396</i>	OL-GLASS			Gm/CF	00000 rininini
11.E MINUTES/CYCLE NINUTES/CYCLE NO NPHW NP NP NP NP NP NP NP NP NP NP NP NP NP	FIG.	NT PROTOC		NT WASH	HEAGENT	Alconox Alconox Alconox Alconox Alconox
11.E MINUTES/CYCLE NINUTES/CYCLE NO NPHW NP NP NP NP NP NP NP NP NP NP NP NP NP	•	EOUIPME		DETERGE	MINUTES	സസസസ
98 HINUT 15555551 15555551		PREP		H RINSE	MbcM	2222
8 HH			ES/CYCLE	PRE WAS	圣	กกกกกก
3408 3408 1 CYCLE CODE 2 SW-3 3 SW-3 5 SW-5 5 SW-5			MINUT		COAD	स्रस्यस्य
40.64 <b>0</b>		3408		CYCLE		98-2-2 88-3 5-4-33
			,			40m4 <b>v</b>

<u>성表表表表</u> TOTAL 9999 UNLOAD COOL PREP EQUIPMENT PROTOCOL-GLASSWARE DRYER 88888 MINUTES ಕಬಬಬಬ 3624 FIG. 36D 222222 88888 3620 2222 3618 CYCLE CODE

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MASHER	
-CARBOY	
PR0T000	
EOUIPMENT	-
딾	

	<b>-</b> .	MINUT	NUTES/CYCLE									
, =	CYCLE	LOAD	PRE WAS NPHW	ASH RINSE NPCW	DETERGE MINUTES	NT REAGENT	Gm/CF	POST WAS	POST WASH BINSE NPHW NPCW	FINAL RINSE	UNLOAD	T0TA
40.624.R	CW-1 CW-2 CW-3 CW-5	<b>22222</b>	22222	~~~~	സസസസ	Alconox Alconox Alconox Alconox Alconox	00000 20000	20000	20000	2222	संसंस्य	

	TOTAL	100 85 85 85 85
	UNLOAD	2222
)Y ORYEA	COOL COOL	88888
COL-CARB(	MINUTES	<b>\$</b> 22222
EQUIPMENT PROTOCOL-CARBOY	ORY TEMP(C)	22222
P EQUIPME	HEAT UP MINUTES	88888
PREP	LOAD	99999
3408	CYCLE	66-2 66-3 6-5
		してひせら

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(As Amended)

FIG. 36G-1 Prep Equipment Protocol-Steam Sterilizer

	, , _b _db						
3606	3608		3610	36	12 3614	36,16	i
		Cycles	7	/			
				SS-1 (			
		Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.	
	•						
1 2 3	Load			·		20	
5 6	Pre Sterilization Deep Vacuum Vacuum/Steam Pulse Vacuum		15	1	1	16	
7 8 9	Steam Subtotal				·.	16	
10 11 12	Sterilization Steam Steam/Air	1	20	40	1		\
13 14	Subtotal					60	
15 16 17 18	Cooling Direct Air Cooling Indirect Jacket Cooling	0	40	. 0	- 1	40	
19 20	Overpressure Subtotal					40	}
21 22 23	Drying Fast Exhaust Slow Exhaust Deep Vacuum	0	20	5	1	25	
24 25 26 27	Vacuum Pulse Heat Heated Pressure						
28 29	Subtotal					25	
30 31	Unload					20	
32	Total Minutes					161	
33	Total Hours					2.7	

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 36G-2

	Г		<del></del>		<del> </del>		<u> </u>				
				SS-2				SS	-3		
	П	Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.	Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.
1						20		·			20
1	$\rangle$		2	0	a	27		<i>,</i>	0	0	27
		1	3	Ö	9	27 18 45	1	3	0	9	27 18 45
١	$\setminus$	1	20	40	1	60	1	20	40	1	60
						60					60
		0	40	0	1	40 40	0 1	40 40	0	1	40 40 80
	\		3	0	10	30	0	20	5	1	25
						30					25
1						20					20
١	H					195 3.3					230 3.8

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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

# FIG. 36H

PREP EQUIPMENT PROTOCOL-DRY HEAT STERILIZER 3408

					•			
	CYCLE	LOAD	HEAT UP MINUTES	STERILI TEMP(C)	ZATION MINUTES	COOL MINUTES	UNLOAD	TOTAL
1 2 2 4 6 5	[30-2	15 15 15 15 15	30 30	250 250 250 250 250 250	25 25	30 30 30 30 30	15 15 15 15	130 115 115 115 115

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 37A

3708	3702	Equipa	ent Prep	Procedur	es		3704		
~	(		EPC1	EPC2	EPC3	EPC4	EPC5	EPCG	EPC7
1 2	Initial Rinse	+							
2 3 4 5 6 7 8	Bench Sink-1 Protocol Duration Hold/Dry Subtotal Cummulative	PHrs. PHrs. PHrs. PHrs.	BS-1 0.33 0 0.33 0.33	BS-1 0.33 0 0.33 0.33	BS-2 0.33 0 0.33 0.33	BS-1 0.33 0.33 0.33	0.00 0.00	0.00	0.00 0.00
9 10 11 12 13 14 15	Wash Station-1 Protocol Duration Hold/Dry Subtotal Cummulative	Plirs. Plirs. Plirs. Plirs.	0.00 0.33333	0.00 0.33333	0.00 0.33333	0.00 0.33333	WS-1 0.25 0.25	WS-1 0.25 0.25	0.00 0
16	Cleaning	-		1,0000					
17 18 19 20 21 22 23 24 25 26 27 28 30 31 32 33 34 35 36 37 38	Bench Sink-1 Protocol Duration Hold/Dry Subtotal Cummulative	PHrs. PHrs. PHrs. PHrs.	BS-3 0.33 0.33 0.66667	BS-3 0.33 0.33 0.66667	BS-4 0.33 0.33 0.66667	0.00 0.33333	0.00 0	0.00 0	0.00 0
25 26 27 28 29 30	Glassware Washer-1 Protocol Duration Hold/Dry Subtotal Cummulative	PHrs. PHrs. PHrs. PHrs.	0.00 0.66667	0.00 0.66667	0.00 0.66667	GW-1 0.67 0.67	0.00	0.00	0.00
32 33 34 35	Glassware Dryer-1 Protocol Duration	PHrs.	GD-1 2.00	6D-1 2.00	60-2 1.75	6D-3 1.75	4.	•	,
39	Hold/Dry Subtotal Cumulative	PHrs. PHrs. PHrs.	2.00 2.66667	2.00 2.66667	1.75 2.41667	1.75 2.75	0.00 0	0.00	0.00 0
40 41 42 43	Carboy Washer-1 Protocol Duration Hold/Dry	PHrs. PHrs.	÷				CV-1 0.25	CW-1 0.25	
44	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.25	0.25	0.00

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 37B

#### Equipment Prep Procedures

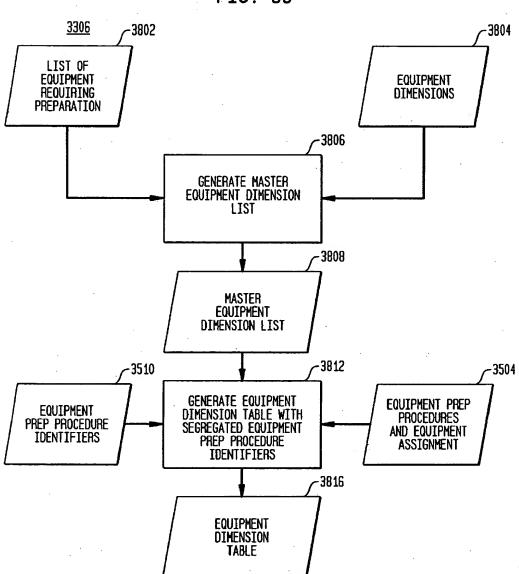
		·							
	- -		EPC1	EPC2	EPC3	EPC4	EPC5	EPC6	EPC7
45 46	Cummulative	PHrs.	2.66667	2.66667	2.41667	2.75	0.25	0.25	0
47 48 49 51 53 53	Carboy Dryer-1 Protocol Duration Hold/Dry Subtotal Cummulative	PHrs. PHrs. PHrs. PHrs.	0.00 2.66667	0.00 2.66667	0.00 2.41667	0.00 2.75	CD-1 1.67 1.67 1.91667	CD-1 1.67 1.67 1.91667	0.00
54	Prep								
55 56	Staffing		2	2	2	2	2	2	2
57 58 59 60 61 62	Preassembly Man Hours Procedure Hours Cummulative	MHrs. PHrs.	2.66667	1 0.5 3.16667	2.41667	2.75	1.91667	1.91667	0
63 64 65 66 67	Wrap Man Hours Procedure Hours Cummulative	MHrs. PHrs.	1.5 0.75 3.41667	1.5 0.75 3.91667	1.5 0.75 3.16667	1.5 0.75 3.5	1.5 0.75 2.66667	1.5 0.75 2.66667	1.5 0.75 0.75
68 69	Sterilization			· · · · ·	·				
70 71 72 73	Autoclave-1 Procedure Duration Hold/Dry	PHrs. PHrs.	SS-1 2.68	SS-1 2.68	SS-1 2.68	SS-1 2.68	SS-2 3.25		SS-3 3.83
74 75	Subtotal Cumulative	PHrs. PHrs.	2.68 6.10	2.68 6.60	2.68 5.85	2.68 6.18	3.25 5.92	0.00 2.67	3.83 4.58
76 77 78 79	Dry Heat-1 Procedure Hours/Load	PHrs.						S0-1 2.17	
80 81 82 83	Hold/Dry Subtotal Cummulative	PHrs. PHrs. PHrs.	0.00 6.10	0.00 6.60	0.00 5.85	0.00 6.18	0.00 5.92	2.17 4.83	0.00 4.58
83 84 85	Total		6.10	6.60	5.85	6.10	6.17	5.08	4.58
86	Max		2.68	2.68	2.69	2.68	3.25	2.17	3.83

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600 For: Method for Scheduling Solution Preparation in

Biopharmaceutical Batch Process Manufacturing





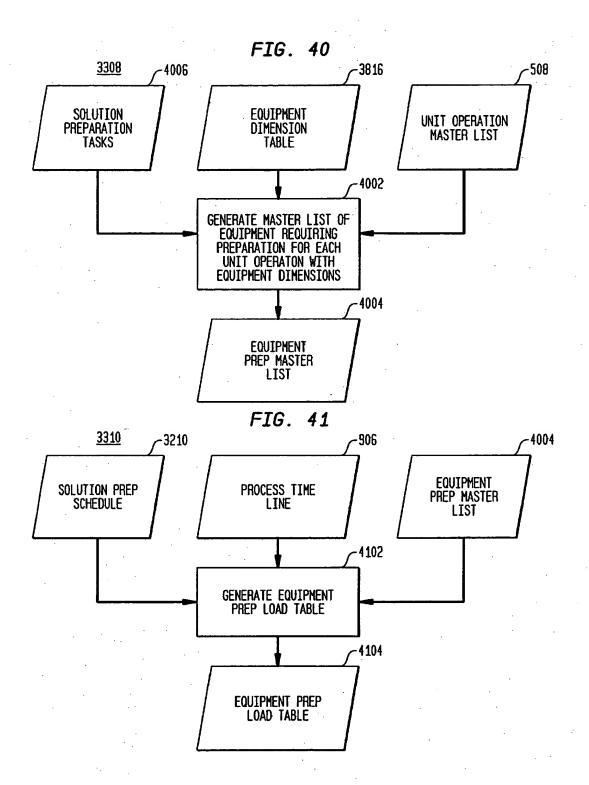
Replacement Sheet
Sheet 58 of 167
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

•	/	_					,							
			$\sim$	Clamps	1.5	0.01							la la	۱̈́٦
			·	$\vdash \vdash$	800	270.				ွှ	451	25 24 35 35 35 35 35	14 18432 18 10.67	_
				Hose Barbs					بو	<b>BSG Carboys</b>	₹.	2424	9424 33 4.88	3952
				-	900	25.0		3910	9-04 <u>3</u>	8	티	32.42	2 2304 7 1.33	
•				Reducers	979			SS.			421	998	4 18432 5 10.67	
				Elbows Crosses		92.0			r.	arboys	2	555	4 6424 3 4.65	3920
	rai			) SMOQ	404	0.033			EPC-5	o PP C	昌	5 6 6	2 2304 5 1.33	
	le-Gene		Fitting	Tees E1	9 7 4	<del>2</del> 66	1			Glassware PP Carboys	Medium	•	0.25	
. 39	Load Configuration Table-General		ш.	pH Probe 1	4~5	90.0		_	EPC-4	Small 61	Small	നനധ	0.98 9.00	3918
FIG	nfigurat		ints	00 Probe pH	400	98.0		3908		_	Large	22.23	3760 0.33	
	Load Co	EPC-2	Instruments	PI 00	4.0.9	.03 8 8 8 8 8				Flexible Tubing	Small	12 4	0.33	3916
				٦		0.00	ا				Bulyl S	446	0.00	
	3905	-	Glass	8	4 2 2	88	1	.		Rubber Stoppers		2 2 2	m 00	3914
		1	Specialty Glass	Siphon Tubes		0		3306		Rubbe	Sloome		0	
		[PC-1	Spec	SE	, , , , , , , , , , , , , , , , , , ,		IJ			SWare	Medium	6 12	432 0.25	
₹.					R/L Inches FIB Inches TIB Inches				FPC-3	Plasticware	Small	നനധ	0.03	3912
		_		$\dashv$	4004 EFF	- 2.0 - 2.2	$\mathbf{I}$			<b>ب</b>				•
	<b>!</b>			—- <u>L</u>	3904		,				٠.			
				-										

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

## FIG. 42A-1

		LIG.	, 42A	L			
4202	4204	Equipment	Prep Load	Table	4206		4208
	Unit	Oper	EPC-1		(,	EPC-2	
·	End	Time	Speciality	Glass		Instru	nents /
Task	Date	Time	Siphon Tubes		: Total	PI 0.03	DO Probe 0.06
1 Inoculum Prep	06/04/96	02:30 PM			0		
2 Flask Growth	06/05/96	01:30 PM	·		0		\
3 Seed Fermentation	06/06/96	03:30 PM	·		.0		
4 Fermentation	06/07/96	12:00 PM			0	4 0.111	
5 Heat Exchange	06/07/96	01:00 PM			0	3	. )
6 Cont. Cent/Solids	06/07/96	11:51 AM			0	0.083	
1 Inoculum Prep	06/06/96	02:30 PM			0	0.300	
2 Flask Growth	06/07/96	01:30 PM			0		
3 Seed Fermentation	06/08/96	03:30 PM			0		
4 Fermentation	06/09/96	MA 00:E0		., .,	. 0	0.111	/
5 Heat Exchange	06/09/96	10:00 AM			0	0.083	
6 Cont. Cent/Solids	06/09/96	08:51 AM			0	3 0.083	
1 Inoculum Prep	06/08/96	02:30 PM			0		7
2 Flask Growth	06/09/96	01:30 PM			0		
3 Seed Fermentation	06/10/96	03:30 PM			0		7
4 Fermentation	06/03/96	10:00 AM	·		0	0.111	
5 Heat Exchange	06/11/96	09:00 AM			0	0.083	. /
6 Cont. Cent/Solids	06/11/96	08:51 AM			0	3 0.083	
7 Cell Resuspension	06/11/96	12:15 PM			. 0	0.000	
B Heat Exchange	06/11/96	09:33 AM			0		
9 Cell Disruption	06/11/96	09:51 AM			0		$ \rangle$
10 Heat Exchange	06/11/96	10:09 AM			0		

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

FIG. 42A-2 Equipment Prep Load Table

_				-qorpc.	it rieb roa	u 10010			
$\mathcal{L}$									EPC-3
$\mathcal{L}$		Fittin	gs	···		-	··, · · · · ·	Total	Plasticware
	pH Probe 0.06	Tees 0.03	Elbows	Crosses	Reducers 0.01	Hose Barbs 0.01	Clamps 0.01	CF	Beakers
)	0.06	0.03	0.02	0.06	0.01	0.01	0.01		0.03
F									
(			[					0.00	
abla									
)					<del></del>			0.00	
	·						•	0.00	
		6 0.17			2	4	16		
\					0.03	0.03	0.17	0.50	*
		0.11				0.03	0.08	0.22	
		4				4	8	U.LL	
Н		0.11				0.03	0.08	0.31	
)								0.00	
Н								0.00	
								0.00	
$ \cdot $									
Ж		6			3	4	16	0.00	
Ш		6 0.17			0.03	0.03	0.17	0.50	
$\setminus$		4				4	8		
Н		0.11				0.03	0.08	0.31	
		0.11				0.03	8 0.08	0.31	
$\langle \Box$									
Н								0.00	
$\rangle$				l	. *			0.00	
Π									
Н				·	_			0.00	
N	•	6 0.17			0.03	0.03	16 0.17	0.50	
/1		4			0.03	4	8	0.30	
Ц		0.11				0.03	0.08	0.31	
		0.11	}			0.03	8 80.0	0.31	
H		V. II				0.03	<u> </u>	0.31	
Д								0.00	
$\langle \  $					1				7
A			<del>  </del>					0.00	
								0.00	
П									
Ч				i	1		i	0.00	·

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 42B-1

4210

				4211	<u>,                                      </u>	•
Unit	Oper .			. 7		
End	Time		Rubber Sto	ppers		ubing /
Date	Time	Flasks 0.25	Silicone 0.00	Butyl 0.03	Silicone 0.33	Neoprene 3.33
06/04/96	02:30 PM					
06/05/96	01:30 PM					\ \
06/06/96	03:30 PM		0.02		1.33	. /
06/07/96	12:00 PM		4		4	
06/07/96	01:00 PM					
06/07/96	11:51 AM					
06/06/96						
06/07/96	01:30 PM					
06/08/96	03:30 PM					
06/09/96						
06/09/96					÷	
06/08/96	02:30 PM					
06/09/96	01:30 PM					
06/10/96	03:30 PM					
06/03/96	10:00 AM					
06/11/96	09:00 AM			•		
06/11/96	08:51 AM					
06/11/96	12:15 PM					
06/11/96	09:33 AM					
06/11/96	09:51 AM					
06/11/96	10:09 AM					
	End Date  06/04/96  06/05/96  06/05/96  06/07/96  06/07/96  06/07/96  06/07/96  06/08/96  06/09/96  06/09/96  06/09/96  06/09/96  06/09/96  06/10/96  06/11/96  06/11/96  06/11/96	06/04/96 02:30 PM 06/05/96 01:30 PM 06/06/96 03:30 PM 06/07/96 12:00 PM 06/07/96 01:00 PM 06/07/96 02:30 PM 06/07/96 01:30 PM 06/08/96 03:30 PM 06/08/96 03:30 PM 06/09/96 03:30 PM 06/09/96 03:30 PM 06/09/96 03:30 PM 06/09/96 01:30 PM 06/09/96 01:30 PM 06/09/96 01:30 PM 06/09/96 03:30 PM 06/10/96 03:30 PM 06/11/96 03:30 PM	End Time  Date  Time  Flasks 0.25  06/04/96  02:30 PM  06/05/96  01:30 PM  06/07/96  12:00 PM  06/07/96  11:51 AM  06/07/96  01:30 PM  06/07/96  01:30 PM  06/07/96  01:30 PM  06/07/96  01:30 PM  06/07/96  03:30 PM  06/09/96  03:30 PM  06/09/96  03:30 PM  06/09/96  03:30 PM  06/09/96  03:30 PM  06/09/96  03:30 PM  06/09/96  03:30 PM  06/09/96  03:30 PM  06/10/96  03:30 PM  06/10/96  03:30 PM  06/10/96  03:30 PM  06/10/96  03:30 PM  06/10/96  03:30 PM  06/10/96  03:30 PM	End Time	Unit Oper End Time	Unit Oper End Time

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Inventor: Peter G. BROWN; Tel. No: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

# FIG. 42B-2

					10.	TLU	_					
			4212						-4214	4216	;	
<i></i>		EPC-4	(		EPC-5				EPC-6			
<u> </u>	Total	Small Gl		Total	PP Carb	,	,	Total	BSG Car		<del>,</del>	Total
	CF	Beakers 0.03125	Flasks 0.25	CF	10L 1.3333	20L 4.88	45L 10.7	CF	10L 1.3333	20L 4.88	45L 10.7	CF 
<i></i>			5									
$\leftarrow$	0.00		5 1.25	1.25				0.00				0.00
\	0.00		5 1.25	1.25				0.00			-	0.00
_	1.35		1.00	1				0.00				0.00
	1.35			0	5.33			5.33				0.00
	0.00			0				0.00				0.00
	0.00			0				0.00	*			0.00
)	0.00		5 1,25	1.25				0.00				0.00
	0.00		5 1.25	1.25	,			0.00	<u> </u>			0.00
_	0.00			0				0.00				0.00
	0.00		_	0				0.00				0.00
/_	0.00			0				0.00	·			0.00
	0.00			0	,			0.00				0.00
	0.00		1,25	1.25				0.00				0.00
	0.00		5 1.25	1.25			·	0.00				0.00
	0.00			0				0.00				0.00
	0.00	-		0				0.00				0.00
	0.00			0				0.00				0.00
	0.00			0				0.00				0.00
	0.00			0				0.00				0.00
	0.00			0				0.00				0.00
	0.00		· 	0				0.00				0.00
	0.00		1.25	1.25				0.00				0.00

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

		Equipment	Prep Load	Table	42,18		4220
		Oper	EPC-1			EPC-2	
	End	Time	Speciality	Glass		Instru	
Equipment Items	Date	Time	Siphon Tubes		Total	PI 0.03	DO Probe 0.08
8 Heat Exchange	06/11/96	10:27 AM	,		0		
9 Cell Disruption	06/11/96	10:45 AM			0		
10 Heat Exchange	06/11/96	12:00 AM			0		
8 Heat Exchange	06/11/96	02:21 PM			0		
9 Cell Disruption	06/11/96	02:39 PM			0		
10 Heat Exchange	06/11/96	02:57 PM	,		0		
11 IB Resuspension	06/11/96	10:57 AM			0		<u> </u>
12 Centrifugation	06/11/96	11:33 AM			0		
11 IB Resuspension	06/11/96	03:06 PM			0		
12 Centrifugation	06/11/96	03:12 PM			0		
13 Renaturation	06/12/96	08:43 AM			0		
14 Buffer Exchange 15 Clarification	06/12/96	11:47 AM			0		/
	06/12/96 06/12/96	11:03 AM 03:59 PM			. 0		
16 Chromatography 1 17 Chromatography 2	06/12/96				0		
18 Buffer Exchange	06/12/96	08:27 PM			0		
19 Chromatography 3	06/12/96	10:07 PM			0		<u> </u>
20 Buffer Exchange		10:38 PM			0		-1
21 Chromatography 4	06/13/96	•			0		<del> </del>
22 Sterile Filtration		12:48 AM	9		.0		
Totals							

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

#### FIG. 42C-2

Fouriement Pren Load Table

		4220	h	Equipme	nt Prep Lo	ad Table			
$\mathcal{L}$		(							EPC-3
$\mathcal{L}$		Fittin	gs					Total	Plasticware
$\cdot \setminus$	pH Probe 0.06	Tees 0.03	Elbows 0.02	Crosses 0.06	Reducers 0.01	Hose Barbs 0.01	Clamps 0.01	CF	Beakers 0.03
f					·			0.00	
1							<u>_</u>	0.00	······································
			-					0.00	
								0.00	
	·							0.00	
								0.00	·
$\rangle$								0.00	
$\langle  $				<del></del>				0.00	
$\cdot$								0.00	
$\mathcal{A}$								0.00	
$\left.\right\rangle$			,					0.00	
A								0.00	
$\forall$	· .						· · · ·	0.00	
								0.00	
1							<u> </u>	0.00 0.00	
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								0.00	
				·				0.00	
								0.00	
								3.25	·

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

FIG. 42D-1 Equipment Top Load Table

4222

			t Top Load		9220	•	
	Unit	Oper Time			7-		
	End	Time		Rubber Sto	ppers	Flexible 1	ubing
Equipment Items	Date	Time	Flasks 0.25	Silicone 0.00	Butyl 0.03	Silicone 0.33	Neoprene 3.33
8 Heat Exchange	06/11/96	10:27 AM		-		*	
9 Cell Disruption	06/11/96	10:45 AM	_				
10 Heat Exchange	06/11/96	12:00 AM					- /
8 Heat Exchange	06/11/96	02:21 PM					
9 Cell Disruption	06/11/96	02:39 PM					
10 Heat Exchange	06/11/96	02:57 PM					. (
11 IB Resuspension	06/11/96	10:57 AM					
12 Centrifugation	06/11/96	11:33 AM					
11 IB Resuspension	06/11/96	03:06 PM					
12 Centrifugation	06/11/96	03:12 PM					/
13 Renaturation	06/12/96	08:43 AM		· · ·			
14 Buffer Exchange	06/12/96	11:47 AM					$ \rangle$
15 Clarification	06/12/96	11:03 AM					
16 Chromatography 1	06/12/96	03:59 PM					$\overline{}$
17 Chromatography 2	06/12/96	06:59 PM			·		
18 Buffer Exchange	06/12/96	08:27 PM					
19 Chromatography 3	06/12/96	10:07 PM					
20 Buffer Exchange	06/12/96	10:38 PM				-	(.
21 Chromatography 4	06/13/96	12:14 AM					$ \rangle$
22 Sterile Filtration	06/13/96	12:48 AM					
Totals				·			
	·			L	L		

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Sheet 67 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

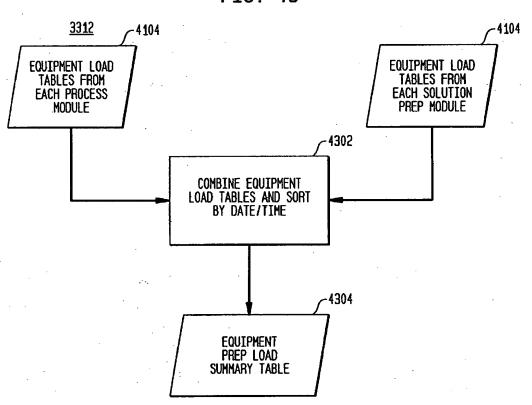
FIG. 42D-2

			4224	Equi	pment To	p Load	i Tabl	.e	4226	4228	}	
		EPC-4	<del>/</del> ·		EPC-5			-	EPC-6	7		
	Total	Small Gl	assware	Total	PP Carbo	oys		Total	BSG Carl	boys		Total
	CF	Beakers 0.03125	Flasks 0.25	CF	10L 1.3333	20L 4.88	45L 10.7	CF	10L 1.3333	20L 4.88	45L 10.7	CF
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

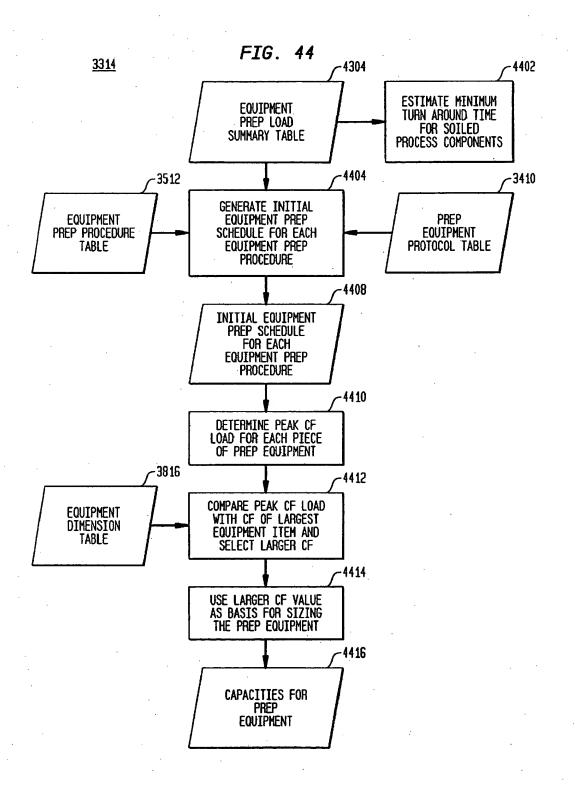




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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600

Inventor: Peter G. BROWN; Tel. No.: 202-371-2000
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing



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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45A-1

OC Load Table-PE Module

		4502 O	C Load Tab	le-PE Modui	le	4504			
		4302				7.	<u> </u>		_
١		•					QA/QC		es
1		0		art	Fin		Vis		H
-		Operation	Date 06/03/96	Time 08:00 AM	Date	Time	WA-T	AV-2	Н
	4	1 A Inoculum Prep	00/03/30	00:00 Ari					Н
	1	T A Thocorom Fi ep			•				1
	3	Set Up	06/03/96	09:30 AM	06/03/96	12:30 PM			(
	4	Preincubation	06/03/96	12:30 PM	06/03/96	03:30 PM			
	23456	Incubation Clean Up	06/03/96 06/04/96	03:30 PM 02:30 PM	06/04/96 06/04/96	02:30 PM 02:45 PM			
-	6	Subtotal	00/01/30	0E.30 TH	00/01/30	02.10 111			H
ı	7						·		Ц
١	8	2 A Flask Growth					,		11
	10	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM			
١	11	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM 01:30 PM			
١	12	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM	\		11
١	13	Clean Up Subtotal	06/05/96	01:30 PM	06/05/96	01:45 PM			Н
-	13 14	Suprorat							
	15 16	3 A Seed Fermentation							$\mathbb{R}$
	17	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM			$  \cdot  $
	18	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM			1)
١	19 20	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		2	$\parallel \parallel$
	20	Harvest CIP	06/06/96 06/06/96	10:30 AM 10:30 AM	06/06/96 06/06/96	11:00 AM 11:30 AM	ŀ		17
ı	22	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM			И
ı	21 22 23	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM			Ц
1	24 25	Subtotal							
	26	4 A Product Fermentation	·						П
-	27 28	Set Ua	06/06/96	09:00 AM	06/06/96	10:00 AM	]		П
-	29	Set Up Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM			I(
-	30	Fermentation	1 36/36/36	11:00 AM	06/07/96	MA 00:80	1	2	П
	31	CIP SIP	06/07/96 06/07/96	08:00 AM 09:00 AM	06/07/96 06/07/96	09:00 AM 10:00 AM			
-	33	Clean Up	06/07/36	10:00 AM	06/07/96	12:00 PM	1		II
	34	Subtotal	05.0.750	20100 3111	00/0//00		<b>i</b>		Н
	35 36	5 A Heat Exchange							H
Ì	37								1
	38	Set Up	06/07/96	MA 00:80	06/07/96	08:30 AM			1
	39 40	Transfer CIP	06/07/96 06/07/96	MA 00:80 MA 00:60	06/07/96 06/07/96	09:00 AM 10:00 AM			
	41	ŠÎP	06/07/96	10:00 AH	06/07/96	11:00 AM			1
	42	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 PM			Ц
	43 44	Subtotal							$\mathbb{N}$
	45	6 A Cont. Cent./Solids							$\prod$
	46 47	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM	1		

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45A-2 OC Load Table-PE Module

4506

Chemical Biochemical Immulogical Act C-1 AC-2 AC-3 AC-4 AC-5 AC-6 AB-1 AB-2 AB-3 AB-4 AB-5 AB-6 AB-7 AI-1 AI-2 AA-4 AB-5 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AB-7 AI-1 AI-2 AB-6 AI-1 AB-1 AI-1 AI-2 AB-6 AI-1 AB-1 AI-1 AI-2 AB-6 AI-1 AI-1 AI-2 AB-6 AI-1 AI-1 AI-2 AB-6 AI-1 AI-1 AI-2 AB-6 AI-1 AI-1 AI-2 AI-1 AI-1 AI-2 AI-1 AI-1 AI-1 AI-1 AI-1 AI-1 AI-1 AI-1		<del></del>	<del></del>		- (		<del></del>		<del></del>							
	Chem	ical					Bioch	emical						Immul	ooical	Act.
	AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
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Dkt No.: 1606,0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

### FIG. 45B-1 OC Load Table-PE Module

		,	·	· · · · · · · · · · · · · · · · · · ·		04.400	01
1		Start		Finish		QA/QC Samples Visual	
	Operation	Date	Time	Date	Time		AV-2
<b></b>	Oper action	06/03/96	08:00 AM	Date	LTING	71-1	74-5
48 49 50 51 52	Centrifugation Wash CIP SIP Clean Up	06/07/96 06/07/96 06/07/96 06/07/96 06/07/96	09:00 AM 10:00 AM 10:06 AM 10:21 AM 11:21 AM	06/07/96 06/07/96 06/07/96 06/07/96 06/07/96	10:00 AM 10:06 AM 10:21 AM 11:21 AM 11:51 AM	·	
53	Subtotal						
54 55 56 57 58 59 60	1 B Inoculum Prep  Set Up Preincubation Incubation Clean Up	06/03/96 06/03/96 06/03/96 06/04/96	01:30 PM 02:30 PM 03:30 PM 02:30 PM	06/03/96 06/03/96 06/04/96 06/04/96	02:30 PM 03:30 PM 02:30 PM 02:45 PM		
60	Subtotal						
61 62 63 64 65 67 67	2 B Flask Growth						
	Set Up Preincubation Incubation Clean Up Subtotal	06/04/96 06/04/96 06/04/96 06/05/96	12:30 PM 01:30 PM 02:30 PM 01:30 PM	06/04/96 06/04/96 06/05/96 06/05/96	01:30 PM 02:30 PM 01:30 PM 01:45 PM		
68							
69 70 71 72 73 74 75 76 77	3 B Seed Fermentation  Set Up Preincubation Fermentation Harvest CIP SIP Clean Up Subtotal	06/05/96 06/05/96 06/05/96 06/06/96 06/06/96 06/06/96	11:30 AM 12:30 PM 01:30 PM 10:30 AM 10:30 AM 11:30 AM 12:30 PM	06/05/96 06/05/96 06/06/96 06/06/96 06/06/96 06/06/96	12:30 PM 01:30 PM 10:30 AM 11:00 AM 11:30 AM 12:30 PM 03:30 PM		2
79 80	4 B Product Fermentation						
81 82 83 84 85 86 87	Set Up Preincubation Fermentation CIP SIP Clean Up	.06/06/96 06/06/96 06/06/96 06/07/96 06/07/96 06/07/96	09:00 AM 10:00 AM 11:00 AM 08:00 AM 03:00 AM 10:00 AM	06/06/96 06/06/96 06/07/96 06/07/96 06/07/96 06/07/96	10:00 AM 11:00 AM 08:00 AM 09:00 AM 10:00 AM 12:00 AM		2
88 89	Subtotal				•		1/
90 91 92	5 B Heat Exchange	00/07/00	00.00 44	00/07/00	00.20 44		
93 94	Set Up Transfer CIP	06/07/96 06/07/96 06/07/96	08:00 AM 08:00 AM 09:00 AM	06/07/96 06/07/96 06/07/96	08:30 AM   09:00 AM   10:00 AM		

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

### FIG. 45B-2

OC Load Table-PE Module 4506

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Chem						Binch	emical			-			Impul	ogical	Act
C-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	Immul AI-1	AI-2	AA-
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45C-1 QC Load Table-PE Module

	·			·				
						QA/QC	Samp1	les
	•	St	ert	Fin	ish	Vis	ual	Г
	Operation	Date	Time	Date	Time	AV-1	AV-2	Г
	0,000	06/03/96	08:00 AM					$\Box$
95	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM		-	Н
96	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 AM			П
		06/0//36	11:00 AM	06/0//36	01:00 AU	<b></b>	-	H
97	Subtotal				•	<b>!</b>	-	П
98	6 B Cont. Cent/Solilds	<del></del>			·	-		Н
99 100	6 6 Cont. Cent/Sollins		i			1		'
101	Sat Ila	06/07/96	MA 00:80	06/07/96	09:00 AM			[
102	Set Up Centrifugation	06/07/96	08:00 AM	06/07/96	10:00 AM			Н
103	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM			17
104	CIP	06/07/96	10:06 AM	06/07/96	10.00 AII			H
105	SIP	06/07/96 06/07/96	10:21 AM	06/07/96 06/07/96	10:21 AM 11:21 AM	1		١١
106	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM	( ·		۱۱
107	Subtotal	30,07,30	TT-CT MI	70171130	TT-OT WIL	}		<del> </del> '
108	Suprorat							L
109	1 C Inoculum Prep	i						H
110	T o Thoogram 11 ch			:				П
111	Set Up	06/03/96	01:30 PM	06/03/96	02:30 PM	ļ		H
112	Preincubation	06/03/96	02:30 PM	06/03/96	03:30 PM			۱١
113	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM			۱۱
114	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM			
114	Subtotal	20,01,00	JE 100 171	70,01,00	JE + 10 111	<del>                                     </del>		$\vdash$
115	20010101	<u> </u>				[		
116	2 C Flask Growth	i						П
117	- Crack Crontil	[						11
118	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM			11
119	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM			۱١
120	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM			ľ
121	Clean Up	06/05/96	01:30 PM	06/05/96	01:30 PM 01:45 PM			
121	Subtotal							Н
122		<u> </u>				[		Ц
123	3 C Seed Fermentation							Π
124					•	,		١١
125	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM			۱١
126	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM			ľ
127	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		٠, ١	
128	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM		2	H
129	CIP	l 06/06/96 l	10:30 AM	06/06/96	11:30 AM			И
130	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM		.	11
131	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM			П
132	Subtotal							Ц
133 l								
134	4 C Product Fermentation			ļ				H
135							ĵ	П
136	Set Up	06/06/96	MA 00:60	06/06/96	10:00 AM			П
137	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM			1(
138	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM		2	1
139	CIP	06/07/96	08:00 AM	06/07/96	MA 00:20		۲	١ ١
140	ŞIP	06/07/96	09:00 AM	06/07/96	10:00 AM			( )
141	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 PM			1

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

# FIG. 45C-2 QC Load Table-PE Module

Chom	ical					Rioch	omical						Tmmul	nniral	Art
C-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AT-1	ogical AI-2	AA-
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Dkt No.: 1606.0020004; Group Unit: 2128
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For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45D-1 QC LOAD TABLE-PE MODULE

		<u>ic load tabi</u>	<u>LE-PE MODUL</u>	<u>E</u>				
						QA/QC	Sampl	es
[	•	Sta	art	Fin	ish	Vis	ual	
ĺ	Operation	Date	Time	Date	Time	AV-1	AV-2	$\neg$
		06/03/96	08:00 AM					7
142	Cubicial	00703730	00.00 /41		<del></del>		-	7
143	Subtotal	ļ					1	
144	5 C Heat Exchange							7
145	5 o near exchange					ļ		1
146	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM	1		1
147	Transfer	06/07/96	MA 00:80	06/07/96	09:00 AM	1		)
148	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM	1		- 1
149	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM	ļ	[ ]	1
150	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 PM	1	[	
151	Subtotal							П
152						<u> </u>		Ц
153	6 C Cont. Cent./Solids				•	]		1
154						}		
155	Set Up	06/07/96	08:00 AM	06/07/96	MA 00:00	1	1	1
156	Centrifugation	06/07/96	09:00 AM	06/07/96	10:00 AM			
157	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM			1
158	CIP	06/07/96	10:05 AM	06/07/96	10:21 AM	l		(
159	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM			1
160	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM			$\Box$
161	Subtotal	ł						
162	7.40	<del> </del>					<del>                                     </del>	Н
163	7 A Resolubilization		ļ			l		1
164	0.4 11.	00103100	00 00 44	00107100	40 00 44	1		1
165	Set Up	06/07/96	09:06 AM	06/07/96	10:05 AM	1		1
166	Dilution	06/07/96	10:06 AM	06/07/96	10:36 AM	ł	]	$\Lambda$
167	Agitate CIP	06/07/96 06/07/96	10:36 AM 11:36 AM	06/07/96 06/07/96	11:36 AM 12:36 PM			1
168	SIP	06/07/96	12:36 PM	06/07/96	01:36 PM			
169 170	Clean Up	06/07/96	01:36 PM	06/07/96	02:36 PM			
171		00/0//38	01.30 111	00/0//30	02.30 TH	<del> </del>		Н
172	Subtotal						•	1
173	8 A Heat Exchange	<del> </del>					l	Ħ
174	o it near Examonge					1.		١ ١
175	Set Up	06/07/96	11:06 AM	06/07/96	11:36 AM		1 1	}
176	Transfer	06/07/96	11:36 AM	06/07/96	11:54 AM	}	t 1	
177	CIP	06/07/96	11:54 AM	06/07/96	11:54 AM	l	l I	1
178	ŠĪP	06/07/96	11:54 AM	06/07/96	11:54 AM			1
179	Clean Up	06/07/96	11:54 AM	06/07/96	11:54 AM	Į.		t
180	Subtotal							7
181								$\perp$
182	9 A Hommogenization		. '			l	}	)
183	0-4-11:							1
184	Set Up	06/07/96	11:39 AM	06/07/96	11:54 AM	l	1	1
185	Lysis CIP	06/07/96	11:54 AM	06/07/96	12:34 PM			1
186		06/07/96	12:34 PM	06/07/96	12:34 PM			1
187	SIP	06/07/96	12:34 PM	06/07/96	12:34 PM			1
188	Clean Up	06/07/96	12:34 PM	06/07/96	12:34 PM	ļ		Ц
189	Subtotal				\		i i	1
190		<u> </u>	L	L	L	<u> </u>	<u>l</u>	

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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45D-2

Shemical   Shochemical   Sho					-		OC LOA	D TABI	E-PE	MODULE	<u>:</u>					
	Chem	ical		•			Rinch	emical	_					Tomul	ooical	Act
	(C-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

## FIG. 45E-1 OC LOAD TABLE-PE MODULE

		UL LUAD IA	BLE-PE MUU	ULE		100	
	·						Samples
			art		ish		ual
	Operation	Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
191	10 A Heat Exchange						
192	To him hear Exonange						l 17
193	Set Up	06/07/96	12:04 PM	06/07/96	12:34 PM		{
194	Transfer	06/07/96	12:34 PM	06/07/96	12:52 PM		
195	CIP	06/07/96	12:52 PM	06/07/96	12:52 PM 12:52 PM		] [ ]
196	SIP	06/07/96	12:52 PM	06/07/96	12:52 PM		
197	Clean Up	06/07/96	12:52 PM	06/07/96	12:52 PM		1 1
198	Subtotal						
199							/
200	8 B Heat Exchange			·			·  {
201					•	ł	I  \
202	Set Up	06/07/96	12:52 PM	06/07/96	12:52 PM	.} .	}
203	Transfer	06/07/96	12:52 PM	06/07/96	01:10 PM		
204	CIP	06/07/96	01:10 PM	06/07/96	01:10 PM		
205	SIP	06/07/96	01:10 PM	06/07/96	01:10 PM		
206	Clean Up	06/07/96	01:10 PM	06/07/96	01:10 PM	<u> </u>	<b> </b>
207	Subtotal					1	I 11
20B 209	9 B Hommooenization	<u> </u>				1	1
210	9 B Hommogenization	ļ				1	1 ! '
211	Set Up	06/07/96	01:10 PM	06/07/96	01:10 PM	ļ	}
212	Lysis	06/07/96	01:10 PM	06/07/96	01:51 PM		l 1 <i>1</i>
213	CIP	06/07/96	01:10 PM	06/07/96	01:51 PM		[]
214	SIP	06/07/96	01:51 PM	06/07/96	01:51 PM		1 1/
215	Clean Up	06/07/96	01:51 PM	06/07/96	01:51 PM		
216	Subtotal	00/0//30	01.31 111	00/0//30	01.31 111	<del> </del>	<del>                                     </del>
217	วถกเกเลเ					l	•   '
218	10 B Heat Exchange					1	
219	To b the exchange						1 1/
220	Set Up	06/07/96	01:21 PM	06/07/96	01:51 PM	l	1 1/
221	Transfer	06/07/96	01:51 PM	06/07/96	02:09 PM		(
222	CIP	06/07/96	02:09 PM	06/07/96	02:09 PM		l 1\
223	SIP	06/07/96	02:09 PM	06/07/96	02:09 PM		
224 225	Clean Up	06/07/96	02:09 PM	06/07/96	02:09 PM		
225	Subtotal						
226			·			<del></del>	<b>  -/</b>
227	8 C Heat Exchange						[/
228	Cat IIa	00,03,00		00/03/00	00 00 00		(
229	Set Up	06/07/96	02:09 PM	06/07/96	02:09 PM	1	\
230	Transfer	06/0//96	02:09 PM	06/0//96	02:2/ PM	1	\
231	CIP	06/07/96	02:27 PM	06/07/96	03:27 PM		
232 233	SIP Clase Ha	06/07/96	03:27 PM	06/07/96	04:27 PM		/
233	Clean Up	06/07/96	04:27 PM	06/07/96	05:27 PM		$\vdash \vdash \vdash \vdash$
234 235 236	Subtotal						
535	9 C Hommogenization	1.					1
237	2 0 HORNINACHITATION	1					}  \
238	Set Up	06/07/96	02:27 PM	06/07/96	02:27 PM		
239	Lysis	06/07/96		06/07/96	03:07 PM		/
- 30	-,	VUI VI I UU .	AE'E' 111 .	20101130 .	03.07 TH		- •

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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45E-2 LOAD TABLE-PE MODULE

	OC LOAD TABLE-PE MODULE           Chemical         Biochemical         Immulogical         Act.           C-1   AC-2   AC-3   AC-4   AC-5   AC-6   AB-1   AB-2   AB-3   AB-4   AB-5   AB-6   AB-7   AI-1   AI-2   AA-1														
Chem	ical					Bioch	emical		• .				Immul	ogical	Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

## FIG. 45F-1 QC LOAD TABLE-PE MODULE

		QC LOAD T	able-pe mod	ULE				
Г						QA/QC	Sample	25
	1	St	art	Fin	ish		ual	7
	Operation	Date	Time	Date	Time		AV-2	٦
		06/03/96	08:00 AM				-	7
240	CIP	06/07/96	03:07 PM	06/07/96	04:07 PM	<b>†</b>		7
241	SIP	06/07/96	04:07 PM	06/07/96	05:07 PM			
242	Clean Up	06/07/96	05:07 PM	06/07/96	06:07 PM			(
243	Subtotal	1 00707700	00.07 111	00707700	00.07 111	<b></b>		1
244		L						$\mathcal{L}$
245	10 C Heat Exchange	1						7
246								1
247		06/07/96	03:07 PM	06/07/96	03:07 PM	ì	l 1	1
248	Transfer	06/07/96	03:07 PM	06/07/96	03:25 PM	İ		1
249	CIP	06/07/96	03:25 PM	06/07/96	04:25 PM			1
250	SIP	06/07/96	04:25 PM	06/07/96	05:25 PM 06:25 PM			1
251 252	Clean Up	06/07/96	05:25 PM	06/07/96	06:25 PM			4
253	Subtotal	,	,					- [
254	11 A Resolubilization	<del> </del>						7
255	TI W MESSIGNITIZATION	l	į					
256	Set Up	06/07/96	11:52 AM	06/07/96	12:52 PM			{
257	Dilution	06/07/96	12:52 PM	06/07/96	01:22 PM			1
258	Agitate	06/07/96	01:22 PM 01:52 PM	06/07/96	01:52 PM			1
259	CĬP	06/07/96	01:52 PM	06/07/96	01:52 PM			1
260	SIP	06/07/96	01:52 PM	06/07/96	01:52 PM			1
261	Clean Up	06/07/96	01:52 PM	06/07/96	01:52 PM			_[
262 263	Subtotal							l
264	12 A Cont.Cent/Solids						·	1
265 266	Sat IIa	00/07/00	42.53 DM	00/07/00	04.E2 DM		1	1
267	Set Up Centrifugation	06/07/96 06/07/96	12:52 PM 01:52 PM	06/07/96 06/07/96	01:52 PM 02:22 PM	1 .	1	- [
268	Wash	06/07/96	02:22 PM	06/07/96	02:28 PM	]		1
269	CIP	06/07/96	02:28 PM	06/07/96	02:28 PM	i l		1
270	ŠĪP	06/07/96	02:28 PM	06/07/96	02:28 PM			l.
l 271	Clean Up	06/07/96	02:28 PM	06/07/96	02:28 PM			ţ
272	Subtotal							7
273 274	11 B Resolubilization							7
275	TI D HESOTUDITIZATION	1				[		1
1 276	Set Up	06/07/96	02:28 PM	06/07/96	02:28 PM			1
277	Dilution	06/07/96	02:28 PM	06/07/96	02:58 PM	l i		l
278	Agitate	06/07/96	1 02:58 PM	06/07/96	03:13 PM			
279	CĬP	06/07/96	03:13 PM	06/07/96	04:13 PM			1
280	SIP	06/07/96	04:13 PM	06/07/96	05:13 PM			1
281	Clean Up	06/07/96	05:13 PM	06/07/96	06:13 PM			_]
282	Subtotal						T	1
282 283 284 285	12 B Cont.Cent/Solids							1
285			45 45 51					1
586	Set Up	06/07/96	02:13 PM	06/07/96	03:13 PM		- 1	1
287	Centrifugation	06/07/96	03:13 PM	06/07/96	03:43 PM		- 1	1
588	l Wash	06/07/96	03:43 PM	06/07/96	03:49 PM	ı	1	I

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaccutical Batch Process Manufacturing
(As Amended)

mical   I     AC-2   AC-3   AC-4   AC-5   AC-6   AB-1   AB-2   AB-3   AB-4   AB-5   AB-6   AB-7   A	[mmulogica	11 4.4
I AC-2 AC-3 AC-4 AC-5 AC-6 AB-1 AB-2 AB-3 AB-4 AB-5 AB-6 AB-7 A		II AC L
	<u> AI-1   AI-2</u>	AA-
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

## FIG. 45G-1 QC LOAD TABLE-PE MODULE

		UC LOAD TA	BLE-PE MUUL	JLE				_
						QA/QC	Sample	S
				Fin	ish	Vis	ual	7
	Operation	Date	Time	Date	Time		AV-2	7
<u> </u>	oper de l'oir	06/03/96	MA 00:80		1,244			7
200	070			00707100	04 04 04	<del> </del>	<b></b>	-{
289	CIP	06/07/96	03:49 PM	06/07/96	04:04 PM			1
290	SIP	06/07/96	04:04 PM	06/07/96	05:04 PM		l I.	1
291	Clean Up	06/07/96	05:04 PM	06/07/96	05:34 PM			7
292	Subtotal		,			į	ŀ	1
293						ļ		4
294	13 A Resolubilization						i:	-1
295								I
296 297	Set Up	06/07/96	01:28 PM	06/07/96	02:28 PM	1		1
297	Dilution	06/07/96	02:28 PM 02:58 PM	06/07/96	02:58 PM		t I	
298	Ag <u>i</u> tat <u>e</u>	06/07/96	02:58 PM	06/08/96	08:58 AM			1
299	CĬP	06/08/96	08:58 AM	06/08/96	09:58 AM	i		1
300	SIP	06/08/96	09:58 AM	06/08/96	10:58 AM	1	l l·	1
301	Clean Up	06/08/96	10:58 AM	06/08/96	11:58 AM			Ţ
302	Subtotal							7
303								4
304	14 A Concentration				į		l l	1
305						l		(
306	Set Up	06/08/96	06:38 AM	06/08/96	07:38 AM	ĺ	i i	
307	Flush	06/08/96	07:38 AM	06/08/96	08:18 AM	ŀ	i i	1
308	Prime	06/08/96	08:18 AM	06/08/96	08:58 AM		i i	Ì
309	Concentration	06/08/96	08:58 AM	06/08/96	09:58 AM	l		-
310	Dilution	06/08/96	09:58 AM	06/08/96	10:25 AM			İ
311	Wash	06/08/96	10:25 AM	06/08/96	11:19 AM			[
312	Flush	06/08/96	11:19 AM	06/08/96	11:39 AM			(
313	Store	06/08/96	11:39 AM	06/08/96	12:19 PM		1	1
314	CIP	06/08/96	12:19 PM	06/08/96	01:19 PM		h 1	1
315	SIP	06/08/96	01:19 PM	06/08/96	02:19 PM		1 1	1
316	Clean Up	06/08/96	02:19 PM	06/08/96	03:19 PM			-
317	Subtotal	00700.00	00.00	00.00.00		1		7
318	Subtotal							]
319	15 A Microfiltration			,				7
320								1
321	Set Up	06/08/96	10:03 AM	06/08/96	11:03 AM			1
322	Flush	06/08/96	11:03 AM	06/08/96	11:11 AM	1		}
323	Prime	06/08/96	11:11 AM	06/08/96	11:19 AM	Į .		- [
324	Filtration	06/08/96	11:19 AM	1 06/08/96	11:49 AM	ľ		
325	Wash	06/08/96	11:49 AM	06/08/96 06/08/96	11:49 AM			1
326	Regenerate	06/08/96	11:49 AM	06/08/96	11:51 AM		}	U
327	Store	06/08/96	11:51 AM	06/08/96	11.55 AM	l	1 1	1
328	CIP	06/08/96	11:55 AM	06/08/96	11:55 AM 12:55 PM			1
329	SIP	06/08/96	12:55 PM	06/08/96	01:55 PM	l		1
330	Clean Up	06/08/96	01:55 PM	06/08/96	02:55 PM			- [
224		V0/V0/30	OT. JU FIL	00/00/30	OC.JJ FFI	<del> </del>	$\vdash$	$\dashv$
331 332	Subtotal					•		İ
132	16 A P/A MPLC							1
333 334	10 7 177 111 110	ł				1		1
335	Equilibration	06/08/96	10:17 AM	06/08/96	11:24 AM	1		1
336	Foaq Edutitor actou	06/08/96	11:49 AM	06/08/96	12:31 PM	l ·	] ]	1
337	Wash	06/08/96		06/08/96		[		- [
1 33/	11604	1 00100120	י זכיאד בעו	י טטוטטוסט	AT: JE LU	•		•

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 45G-2

					. (	OC LOA	D TABI	LE-PE	MODULE	<u> </u>					
Chem	ical			<del>-</del>		Γ			<del></del>		<del></del>		Immul	ooical	Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
		<u> </u>					<u> </u>	<del> </del>			<u> </u>	<b> </b>			
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Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

		QC LOAD T	ABLE-PE MOD	DULE		· ·		
						QA/QC	Sampl	es
					ish		ual	Ц
<u></u>	Operation	Date	Time	Date	Time	AV-1	AV-2	Ц
		06/03/96	MA 00:80					Ц
338	Elute A	06/08/96	01:52 PM	06/08/96	03:12 PM		İ	17
339	Elute B	06/08/96	03:12 PM	06/08/96	03:12 PM			H-
340	Regenerate	06/08/96	03:12 PM	06/08/96	03:25 PM			١\
341 342	Store CIP	06/08/96	03:25 PM 03:52 PM	06/08/96 06/08/96	03:25 PM 03:52 PM 04:52 PM		,	١\
343	ŠĪP	06/08/96	04:52 PM	06/08/36	05:52 PM			1
344	Člean Up	06/08/96	05:52 PM	06/08/96	06:52 PM		ľ	$\Box$
345	Subtotal	1	70.02	70170702				Π
346		ł				ļ		17
347	43 4 5 4 4 4 5 4 5 4 5 4 5 4 5 4 5 4 5 4					<u> </u>		Н
348	17 A P/A MPLC		•					١١
349 350	Equilibration	06/08/96	02:59 PM	06/08/96	03:38 PM		ŀ	1
351	Load	06/08/96	03:12 PM	06/08/96	03:38 TH			1/
352	Wash	06/08/96	04:17 PM	06/08/96	05:03 PM			17
353	Elute A	06/08/96	05:03 PM	06/08/96	05:49 PM			$\Pi$
353 354 355	Elute B	06/08/96	05:49 PM	06/08/96	05:49 PM			1(
355	Regenerate	06/08/96	05:49 PM 05:57 PM	-06/08/96	05:57 PM 06:13 PM			I١
356 357 358	Store	06/08/96	05:57 PM	06/08/96	06:13 PM	l		1
1 32/	CIP SIP	06/08/96	06:13 PM	06/08/96 06/08/96	07:13 PM 08:13 PM			1 /
359	Clean Up	06/08/96 06/08/96	07:13 PM 08:13 PM	06/08/96	09:13 PM			1/
360	Subtotal	00100130	VO. 13 TH	007 007 30	03.13 111	-		H
361								H
362 363	18 A Flow Dialysis							$  \cdot  $
364	Set Up	06/08/96	03:29 PM	06/08/96	04:29 PM			1 }
365	Flush	06/08/96	03:29 PM 04:29 PM	06/08/96	04:29 PM 05:09 PM			$\Pi$
366	Prime	06/08/96	05:09 PM	06/08/96	05:49 PM			17
367	Dialysis	06/08/96	05:49 PM	06/08/96	06:49 PM			17
368	Wash	06/08/96	06:49 PM	06/08/96	06:49 PM			11
369 370	Flush Store	06/08/96 06/08/96	06:49 PM 07:09 PM	06/08/96 06/08/96	07:09 PM 07:49 PM			١١
371	CIP	06/08/96	07:49 PM	06/08/36	08:49 PM			<b> </b>
371 372	ŠĪP	06/08/96	08:49 PM	06/08/96	09:49 PM			
373	Clean Up	06/08/96	09:49 PM	06/08/96	10:49 PM			-
374	Subtotal							Π
375 376	19 A P/A MPLC							Ħ
377	·		as so su					1
378	Equilibration	06/08/96	05:59 PM	06/08/96	06:31 PM			
379	Load	06/08/96 06/08/96	06:49 PM 07:03 PM	06/08/96 06/08/96	07:03 PM			П.
381	Wash   Elute A	06/08/36	07:03 FM	06/08/96	07:41 PM 08:20 PM			1/
382	Elute B	06/08/96	08:20 PM	06/08/96	08:20 PM			П
382 383	Regenerate	06/08/96	08:20 PM	06/0B/96	08:26 PM			
384	Store	06/08/96	08:26 PM	06/08/96	08:39 PM			
385	- CIP	06/08/96	08:39 PM	06/08/96	09:39 PM			}
386	SIP	06/08/96	09:39 PM	06/08/96	10:39 PM		. 1	1

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

(As Amended)

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Chem	ical					Binch	emical						Tmm:1	ogical	Act
		AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7		AI-2	
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

		QC LOAD TA	ABLE-PE MOD	ULE			
						QA/QC	Samples
	×.			Fin	ish	Vis	ual
<u> </u>	Operation	Date	Time	Date	Time		AV-2
		06/03/96	08:00 AM				
387	Clean Up	06/08/96	10:39 PM	06/08/96	11:39 PM		
388	Subtotal	}					
389							$\sqcup \sqcup$
390	20 A Flow Dialysis	[					
391 392	Cod Ho	00100100	07:00 PM	00100100	07.00 04		
393	Set Up Flush	06/08/96 06/08/96	07:00 PM	06/08/96 06/08/96	07:00 PM 07:40 PM	ŀ	
394	Prime	. 06/08/96	07:40 PM	06/08/36	08:20 PM		
395	Dialysis	06/08/96	08:20 PM	06/08/96	10:20 PM	ľ	l 1 <i>1</i>
396	Wash	06/08/96	10:20 PM	06/08/96	10:20 PM	٠,	(
397	Flush	06/08/96	10:20 PM	06/08/96	10:40 PM	<u> </u>	<i>[</i>
398	Store	06/08/96	10:40 PM	06/08/96	11:20 PM		\
399	CIP	06/08/96	11:20 PM	06/08/96	11:20 PM	İ	
400	SIP Class Ha	06/08/96 06/08/96	11:20 PM 11:20 PM	06/08/96	11:20 PM 12:20 AM		1 1
402	Clean Up	00/00/30	11:20 FM	06/09/96	12:20 AM		$\vdash$
403	Subtotal	Ì					11
404	21 A P/A MPLC						
405							
406	Equilibration	06/08/96	09:28 PM	06/08/96	09:57 PM		
407	Load	06/08/96	10:20 PM	06/08/96	10:26 PM		
408 409	Wash	06/08/96	10:26 PM	06/08/96	11:01 PM		-11
410	Elute A Elute B	06/08/96 06/08/96	11:01 PM 11:36 PM	06/08/96 06/08/96	11:36 PM 11:36 PM		- H
411	Regenerate	06/08/96	11:36 PM	06/08/96	11:30 PM		
412	Store	06/08/96	11:42 PM	06/08/96	11:54 PM		
413	CIP	06/08/96	11:54 PM	06/08/96	11:54 PM		
414	SÍP	06/08/96	11:54 PM	06/08/96	11:54 PM		
415	Clean Up	06/08/96	11:54 PM	06/09/96	12:54 AM		
416	Subtotal	+ 1				,	
417 418	22 A Sterile Filtration						<del></del>
419	zz a sterije Elitration						1.1
420	Set Up	06/09/96	08:06 AM	06/09/96	08:36 AM		
1 421	Filtration	06/08/96	11:36 PM	06/09/96	12:06 AM		1 1
422	Storage	06/09/96	.12:06 AM	06/09/96	12:36 AM		11
1 423	CIP	06/09/96	12:36 AM 12:36 AM	06/09/96	12:36 AM		$\Box H$
424	SIP	06/09/96	12:36 AM	06/09/96	12:36 AM		- [{
425	Clean Up	06/09/96	12:36 AM	06/09/96	01:36 AM		$\Box$
426	Subtotal						$-\Box$
		L					

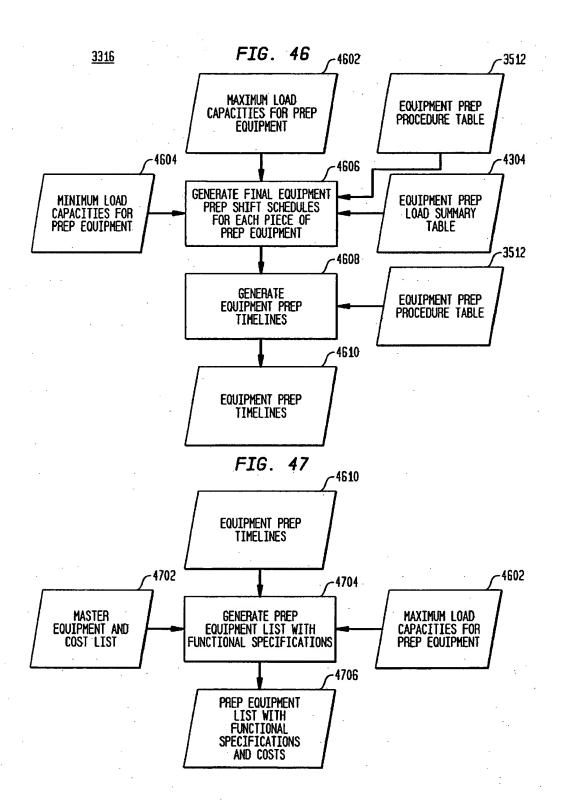
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

Chemical						0	C LOA	D TABL	E-PE I	10DULE			. •			
	Chem	ical					Bioch	emical						Immul	ogical	Act.
	AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing

(As Amended)

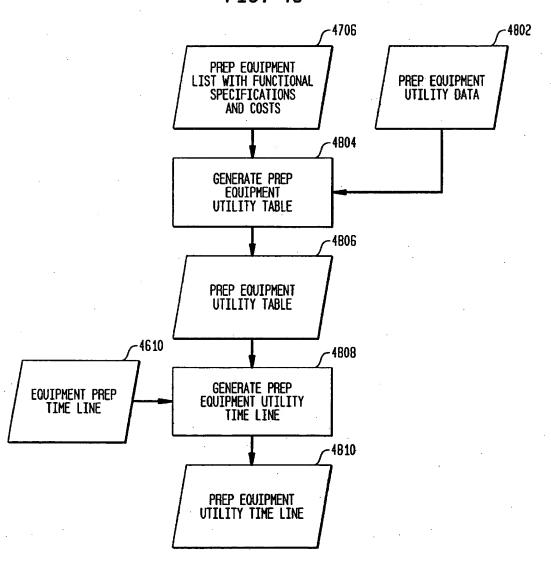


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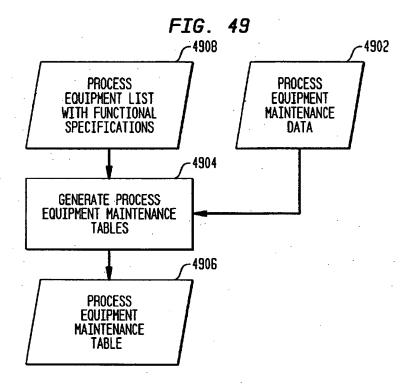
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaccutical Batch Process Manufacturing

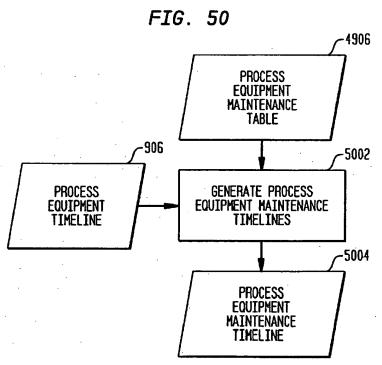
(As Amended)

FIG. 48



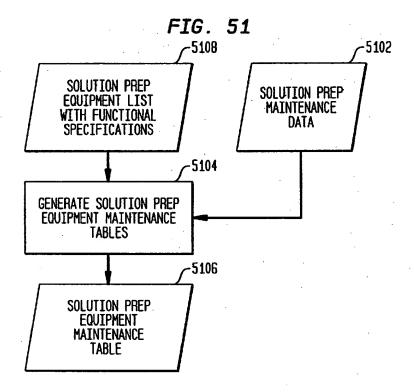
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

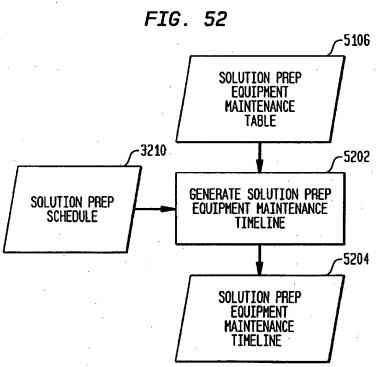




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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)



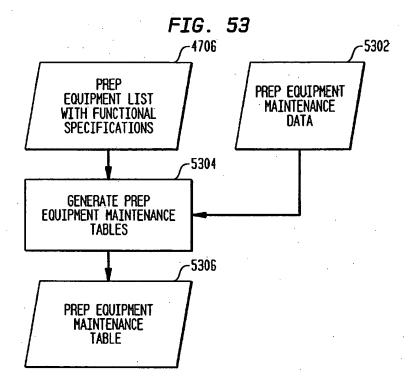


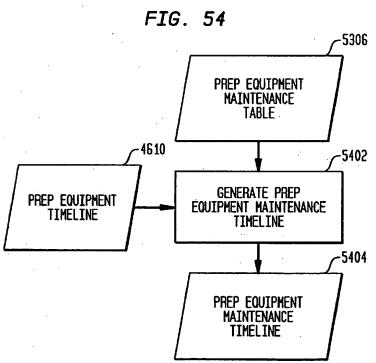
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

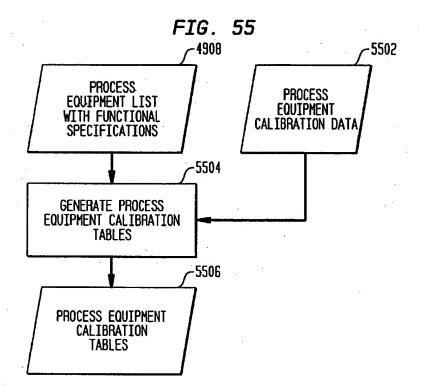
(As Amended)

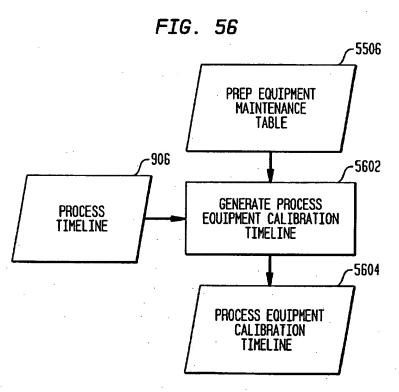




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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

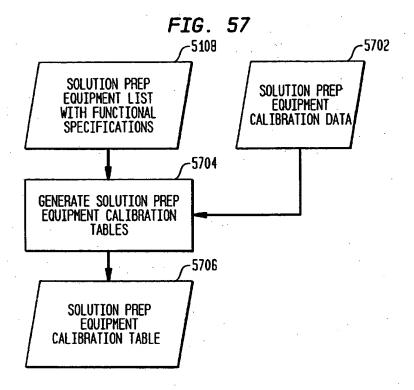


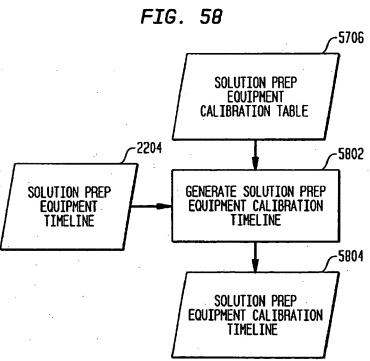


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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing

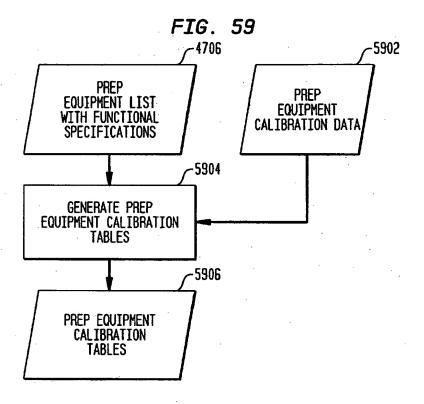
(As Amended)

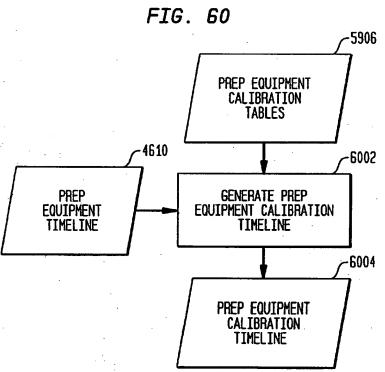




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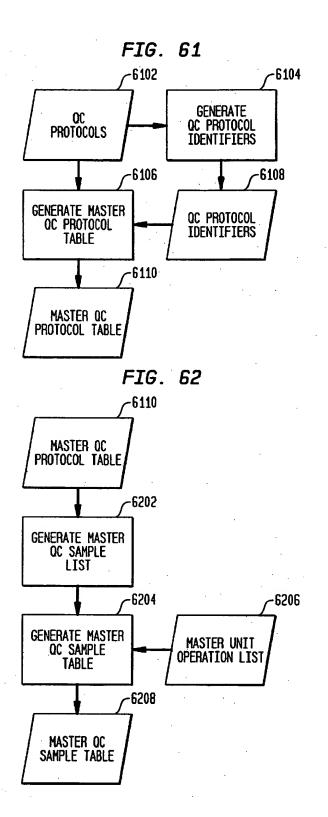
Appl. No.: 09/100,088; Filed: June 19, 1998
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)





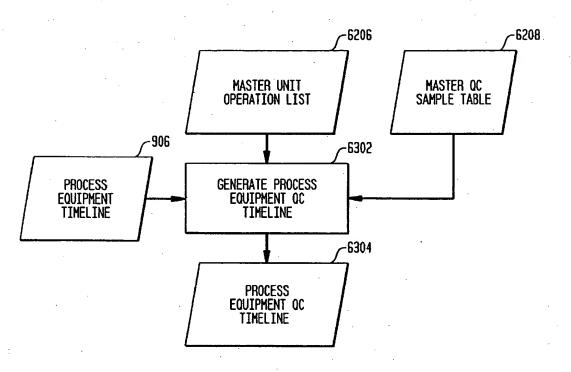
#### Replacement Sheet Sheet 96 of 167 Appl. No.: 09/100,088; Filed: June 19, 1998

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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FIG. 63



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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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(As Amended)

### FIG. 64A-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION 6402 6404

6402	4	-		6404		
	Filters		· <u></u>			$\overline{}$
· ·	Materia	ls				Labor
Equipment Items	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
1 Inoculum Prep						
-80 C Stock Freezer Shaking Water Bath						
2 Flask Growth						
Floor Incubator-Shaker Microscope						[ {
3 Seed Fermentation////						
Seed Bioreactor						· )
4 Fermentation						
Production Bioreactor	75868	1	100	55	.55	.5 \
5 Whole Cell Harvest						
Harvest Heat Exchanger Harvest Vessel						/
Agitator	/////	7777	,,,,,,,,,,	,,,,,,,,	777777	
6 Cell Concentration/// Pump						
Filter Holder						1
Manifolding Instrumentation		•				- 1
MF Flush Vessel					·	. \
MF Prime Vessel			}			1
MF Filtrate Vessel						. /
Agitator						\
MF Wash Vessel				j		)
MF Regeneration Vessel						<i>[]</i>
MF Storage Vessel						(

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(As Amended)

## FIG. 64A-2

		EQUI	PMEN	T MAINTENAN	ICE TABLE-MI 6406	(CROBIAL	FERMENTA	ATION	6408
\		Gaskets			···· (	•			Bearings
		Materia	ls				Labor		Materials
	\$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item No.
		/////	///					/////	//////
<b>Z</b> 4			7//	/////////	(///////	//////		<i>(/////</i>	(//////
	/////	/////						/////	
4		<i>//////</i>	72		(///////	//////	/////	<i>(/////</i>	<i>//////</i>
			///				//////	07///	//////
4	·	//////	Y Z Z		////////	/////	//////	<i>//////</i>	(//////
		77777				/////		/////	
4	.0875	<b>48</b> 994	1	500	55	.11	1	.035	//////
								11111	
4	//////	62589	1	350	85	.2429	1	.05	//////
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## FIG. 64B-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION 6408

		***************************************	6408		
					Labor
Equipment Items	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
1 Inoculum Prep//////	2777	////////		0/////	/////
-80 C Stock Freezer	<i>¥22</i>	(///////	<i>////////</i>	<i>[[]]</i>	
Shaking Water Bath	1				
2 Flask Growth	2000			77777	11111
Floor Incubator-Shaker	X///	/////////	<i>///////</i>		(////
Microscope	1				
3 Seed Fermentation////	1111	///////	////////	777777	77777
	<i>Y///</i>	////////	<i>(////////</i>		/////
Seed Bioreactor					
4 Fermentation///////	1///	V///////	////////		/////
	<i>Y///</i>	<i>[[]]</i>	///////		
Production Bioreactor				-	
5 Whole Cell Harvest	1777	////////	///////	//////	77777
Harvest Heat Exchanger	<i>XZZZ</i>		////////		
Harvest Vessel	1				
Agitator	1				1
6 Cell Concentration////	1///			77777	7////
Pump	X///				
Filter Holder	-				
Manifolding	1	2			
Instrumentation	i				
·			·	·	
MF Flush Vessel	]				
	1				
MF Prime Vessel	ł				
MF Filtrate Vessel					1
					(
Agitator	1.				,
MF Wash Vessel	1	,			
				10-	
MF Regeneration Vessel					i
WE Channe Warrel					(
MF Storage Vessel		·	l	J	\

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#### FIG. 64B-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Seals	•				· · · · · · · · · · · · · · · · · · ·		Belts	
-		Materia	ls	-	——————————————————————————————————————		Labor		Materia	ls
	\$/Cycle	Item No.	Oty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item No	Qt
								, ,		$\vdash$
1										1/2
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		54812 48695	2 1	250 250	12 18.9	.048 .0756	1 1	.07 .07		
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FIG. 64C-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION 6414

	6414									
				Labor						
Equipment Items	Cycle Life	Unit Cost	\$/Cycle	Hours						
1 Inoculum Prep//////		(///////	//////	/////						
-80 C Stock Freezer	<i>///////</i>	<i>[[]]</i>	(/////							
Shaking Water Bath	<b>-</b>									
2 Flask Growth		///////	111111	/////						
Floor Incubator-Shaker	<i>~~~~~~</i>	(///////	Y/////							
Microscope	†									
3 Seed Fermentation				/////						
Seed Bioreactor	<i>(////////////////////////////////////</i>	<u>////////</u>	/////							
occa mini carini										
4 Fermentation	///////	///////	/////	/////						
Production Bioreactor	500	25	.05	1						
Troduction biol cactor	300	LJ	.03	1						
5 Whole Cell Harvest			/////	/////						
Harvest Heat Exchanger	7777777		(/////	/////						
Harvest Vessel			ł	1						
Agitator										
6 Cell Concentration			/////							
Pump	(////////		/////	<u> </u>						
Filter Holder										
Manifolding										
Instrumentation				ı						
				1						
MF Flush Vessel										
MF Prime Vessel			. [							
MF Filtrate Vessel				/						
-			- 1	(						
Agitator			j	/						
MF Wash Vessel										
115.0										
MF Regeneration Vessel										
MF Storage Vessel	,	•		. (						
un arni ade sezzet			1	1						

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#### FIG. 64C-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

				ITTENT TRAIN	6416		JINE II		6418		
		Shafts							Lubrica	nt	
$\mathcal{L}$		Materia					Labor		Materia		
}	\$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item No.	0ty	Cycle Life
k											
									78954	.5	
	.035										
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FIG. 64D-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	6418		
	}		
·		·	Labor
Equipment Items	Unit Cost	\$/Cycle	Hours
1 Inoculum Prep///////			
-80 C Stock Freezer	<i>*///////</i>	//////	11111
Shaking Water Bath	1		· \
2 Flask Growth			/////
Floor Incubator-Shaker	<i>~~~~~~</i>		111114
Microscope			(
3 Seed Fermentation			
Seed Bioreactor	1.5	.03	.5
4 Fermentation////////			
Production Bioreactor		~~~~	
5 Whole Cell Harvest		//////	
Harvest Heat Exchanger	////////	77777	
Harvest Vessel			/.
Agitator			\
6 Cell Concentration			
Pump			\
Filter Holder			· /
Mani folding			
Instrumentation			
MF Flush Vessel			\
MF Prime Vessel			. /
MF Filtrate Vessel			
Agitator			/
MF Wash Vessel			$\rangle$
MF Regeneration Vessel			
MF Storage Vessel			(

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(As Amended)

(As Amended)

## FIG. 64D-2 EQUIPMENT MAINTENANCE TABLE-HICROBIAL FERMENTATION

							64				
\ \		Ther	nal	Med	ia						
Γ	· · · · · · · · · · · · · · · · · · ·	Mate	ria!	ls						Labor	
	\$/Cycle	Item	No.	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle
7		////	<i>77)</i>		7777	7777	7777	////	//////	7777	/////
2											
	//////	7777	,,,	///	7777	,,,,	7777	7777	~~~~	27777	,,,,,,,
4											
		7777	77	77	,,,,,		////	,,,,,	,,,,,,,	////	/////
4	. 175										
	.113	777		,,,		~~~	,,,,,	7777			~~~~
4		5625		5	<u>////</u> 50			<u>////</u> 35	425	1	///// 17.5
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For: Method for Scheduling Solution Preparation in
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#### FIG. 64E-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

:	le					
	Filters					
	Materia	ls				Labor
Equipment Items	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
7 Cell Concentration 2	<i>X/////</i>			<i>}///////</i>		
MF Wash Vessel						
D.,	1					
Pump Filter Holder	-			] .		
Manifolding	-		]		1	
Instrumentation	1					
THE CHARTITECTURE						
MF Flush Vessel	1 .	1		[		
	1	ĺ			<u> </u>	
MF Prime Vessel	}			}		
MF Filtrate Vessel						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						
8 Cell Resuspension	/////	////				/////
Resuspension Vessel	/////				11///	/////
Stir Plate						
9 Cell Disruption/////					/////	
Cell Disruptor	~~~					
Lysate Vessel						
10 IB Resuspension 182///						/////
Resuspension Vessel						
Stir Plate						1
11 IB Concentration 182	/////				/////	
MF Wash Vessel						<u> </u>
Pump			i		}	/
Filter Holder			- 1	'		

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### FIG. 64E-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Gaskets		·		· 				Bearing	JS
		Materia	ls		Labor		Material				
	\$/Cycle	Item No	Oty	Cycle Life	Unit (	Cost	\$/Cycle	Hours	\$/Cycle	Item No	).
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### FIG. 64F-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours				
7 Cell Concentration 2///									
MF Wash Vessel		·							
Pump	1 .		,						
Filter Holder Manifolding	4			<u> </u>					
Instrumentation	†								
MF Flush Vessel	1								
MF Prime Vessel	-								
MF Filtrate Vessel	1				, ,				
MF Wash Vessel		<u> </u>			- (				
MF Regeneration Vessel	1				١				
MF Storage Vessel	1								
8 Cell Resuspension									
Resuspension Vessel					4				
Stir Plate	1111	7777777	(///////	777777	//////				
9 Cell Disruption//// Cell Disruptor									
Lysate Vessel	1								
10 IB Resuspension 162///	1///		///////	/////	77777				
Resuspension Vessel	X///	<i>/////////////////////////////////////</i>	<i>\(\(\(\(\(\(\)\\\\\\\\\\\\\\\\\\\\\\\\</i>	1/////	11114				
Stir Plate	1		1		1				
11 IB Concentration 162//	1///		///////						
MF Wash Vessel	<i>Y///</i>	(////////	<i>(11111111</i>	//////	<u> </u>				
Pump	]				(				
Filter Holder		,			\				

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### FIG. 64F-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Seals									Belts	
		Materia	ls						Labor		Materi	als
	\$/Cycle	Item No.	ûty	Cycle Li	fe	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item No	o.Qt
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FIG. 64G-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

						•
						. )
						Labor
Equipment Items	Cycle L	.i fe	Unit	Cost	\$/Cycle	Hours
7 Cell Concentration 2						
MF Wash Vessel		~~	~///		******	//////
Pump	1					
Filter Holder	]				·	(
Manifolding	1					1
Instrumentation			•			
MF Flush Vessel						
MF Prime Vessel	1					(
MF Filtrate Vessel						\
MF Wash Vessel						/
MF Regeneration Vessel	1					(
MF Storage Vessel						1
8 Cell Resuspension		<i>7</i>				
Resuspension Vessel			<del></del>			
Stir Plate						
9 Cell Disruption						
Cell Disruptor			-4-4-1			
Lysate Vessel						/
10 IB Resuspension 182		//				
Resuspension Vessel		1				and
Stir Plate				l		1.
11 IB Concentration 162//		//	/////		/////	
MF Wash Vessel						.
Pump						/
Filter Holder		- 1				/
		-		•	•	•

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FIG. 64G-2

#### EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Shafts								Lubrica	nt	
		Materia	ls					Labor		Materia	ls	
	\$/Cycle	Item No	.Oty	Cycle Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item No	.Oty	Cycle Li
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	//////	77777	   	///////	\ \(\tau_{1/1/2}\)	////	777777	7777	77777	77777	\ \''	//////
4	//////	//////	1//		<i>X////</i>		//////	////			7//	<i>(///////</i>
	//////	77777	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	////////	, , , , , , , , , , , , , , , , , , ,	,,,,,	77777	7777	,,,,,,,	777777		***********
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(As Amended)

FIG. 64H-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

·			
			Labor
Equipment Items	Unit Cost	\$/Cycle	Hours
			· · · · · · · · · · · · · · · · · · ·
7 Cell Concentration 2	<i>\\\\\\</i>		
MF Wash Vessel			
Pump		·	
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel		·	
MF Prime Vessel			
MF Filtrate Vessel			'
MF Wash Vessel			1
MF Regeneration Vessel			1
MF Storage Vessel			
8 Cell Resuspension			/////
Resuspension Vessel	/////////		
Stir Plate			(
9 Cell Disruption			/////
Cell Disruptor	///////	<u> </u>	
Lysate Vessel		ļ	
10 IB Resuspension 1&2///			/////
Resuspension Vessel			<i>1111</i> 4
Stir Plate		ļ	/
11 IB Concentration 182		<i>77777</i>	m
MF Wash Vessel	<i>([[]]</i>		<u>/////</u>
Pump		ł	/
Filter Holder	·	Ì	1
	ı l	ľ	. 1

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### FIG. 64H-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

					·		·	
		Therma	1 Med	dia				
/		Materi	als				Labor	
1	\$/Cycle	Item No	Oty	Cycle Lif	e Unit Cost	\$/Cycle	Hours	\$/Cycle
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6		7777				\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	7777	777777
K	<i>X/////</i>		24//	<i>[[]][]</i>	<u> </u>	<i>[[]]</i>		
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	<i>Y/////</i>		<b>X</b>		<i>X///////</i>			
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### FIG. 64I-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Filte	ers							
	Mater	ial	S						Labor
Equipment Items	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours
Manifolding						<u> </u>			
Instrumentation									
MF Flush Vessel		-9					÷		
MF Prime Vessel	1	ŀ							
MF Filtrate Vessel									
MF Dilute Vessel									
MF Wash Vessel									
MF Regeneration Vessel									
MF Storage Vessel	Ī								
14 Renaturation									
Renaturant Vessel		-							
Stir Plate	ŀ								,
15 Buffer Exchange		//							
Pump							-		
Filter Holder		İ							
Manifolding								. [	
Instrumentation	İ								
UF Flush Vessel									
UF Prime Vessel									
UF Filtrate Vessel									(
·									
UF Wash Vessel							•	*	
UF Diluent Vessel									
UF Regeneration Vessel						٠.	,		· . (
UF Storage Vessel							- 1		

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### FIG. 64I-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		6askets								Bearings
		Materia	ls					Labor		Material
	\$/Cycle	Item No.	Oty	Cycle Lif	e Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item No.
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### FIG. 64J-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		•					Labor
Equipment Items	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours
Manifolding							
Instrumentation							
MF Flush Vessel		·					
MF Prime Vessel							
MF Filtrate Vessel							
MF Dilute Vessel							
MF Wash Vessel							
MF Regeneration Vessel	,						
MF Storage Vessel							
14 Renaturation					////		
Renaturant Vessel	<del></del>						(
Stir Plate							
15 Buffer Exchange							
Pump				•			
Filter Holder							
Manifolding Instrumentation							
THE FLAME OF TAKEN							
UF Flush Vessel							
UF Prime Vessel							
UF Filtrate Vessel						,	l
							,
UF Wash Vessel	,						
UF Diluent Yessel							
UF Regeneration Vessel	•						(
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### FIG. 64J-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

_		Seals							Belt	S	
_		Materia					Labor		Mate	rial	S
	\$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item	No.	Qty
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### FIG. 64K-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

				Labor
Equipment Items	Cycle Life	Unit Cost	\$/Cycle	Hours
Manifolding				
Instrumentation				'
MF Flush Vessel				
MF Prime Vessel				ı
MF Filtrate Vessel				
MF Dilute Vessel				
MF Wash Vessel				
MF Regeneration Vessel				(
MF Storage Vessel				
14 Renaturation				
Renaturant Vessel				(
Stir Plate				
15 Buffer Exchange				
Pump Filter Holder				
Manifolding				1
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				. (
UF Wash Yessel		*		'
UF Diluent Vessel				,
UF Regeneration Vessel				(
UF Storage Vessel				1

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#### FIG. 64K-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

abla		Shafts							Lubri	cant		
Γ		Materia	ls				Labor	• "	Mater	ials		_
abla	\$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item N	lo . Oty	Cycle Lif	fe
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FIG. 64L-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

			\
			Labor
Equipment Items	Unit Cost	\$/Cycle	Hours
Manifolding	<u> </u>		
Instrumentation			\
MF Flush Vessel			
MF Prime Vessel			1
MF Filtrate Vessel			
MF Dilute Vessel			1
MF Wash Vessel	·		
MF Regeneration Vessel			{
MF Storage Vessel			\
14 Renaturation			
Renaturant Vessel	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		
Stir Plate			
15 Buffer Exchange			
Pump			1
Filter Holder			1
Manifolding			(
Instrumentation			\
UF Flush Vessel			)
UF Prime Vessel			/
UF Filtrate Vessel			
UF Wash Vessel			$\rangle$
UF Diluent Vessel			/
UF Regeneration Vessel		·	. (
UF Storage Vessel			\

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FIG. 64L-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

abla	•	Therma	1 Mec	lia						
$\nearrow$		Materi		*			-		Labor	
	\$/Cycle	Item No	.Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle
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#### FIG. 64M-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Filters		· · · · · · · · · · · · · · · · · · ·			
•						·
	Materia					Labor
Equipment Items	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
UF Waste Vessel						
16 Chromatography 1////						
Chromatography Column						
Pump	<u> </u>					
Inst.& Control System			<b>,</b>			
Manifolding					]	
Equilibration Vessel			•			
Wash Vessel	5				*	
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
17 Chromatography 2////						
Chromatography Column						
Pump	*					
Inst.& Control System				_		
Manifolding						
Equilibration Vessel			}			
Wash Vessel						(
Eluent Vessel				,		
Regenerate Vessel						í

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#### FIG. 64M-2 FOLITPMENT MATNIFNANCE TABLE-MICRORIAL FERMENTATION

	·	Gaskets									Beari	ngs
		Materia	ls				-		Labor		Mater	ial
	\$/Cycle	Item No.	.Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No.
_	<u>.</u>		-									
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FIG. 64N-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		-					Labor
Equipment Items	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours
UF Waste Vessel							,
			,,,,	,,,,	,,,,,	******	****
16 Chromatography 1////					<u> </u>		
Chromatography Column	-						
Pump	]				-		
Inst.& Control System		·					
Manifolding	1						
Equilibration Vessel	]						
Wash Vessel	1						(
Eluent Vessel							
Regenerate Vessel							,
Storage Vessel	1						١
Waste Vessel(1)	1					a	
Product Vessel	1						
Waste Vessel(2)	·			,			
17 Chromatography 2////	1111						
Chromatography Column							
Pump	1						
Inst.& Control System							\
Manifolding	1		·				
Equilibration Vessel							. ,
Wash Vessel							(
Eluent Vessel	1						}
Regenerate Vessel	1						/

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

#### FIG. 64N-2 FOUTPMENT MATNTENANCE TABLE-MICRORIAL FERMENTATION

_		Seal	. <b>S</b>									Belt	S	
		Mate	ria	ls						Labor		Mate	ia.	ls
	\$/Cycle	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No .	0t
-	-		-			•								H
		///		///	////	////	7///	////					///	
1		///	///	22	/////			7777		/////	<i></i>	2222	<i>ZZ</i> .	
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

#### FIG. 640-1 EQUIPMENT MAINTENANCE TARLE-MICRORIAL EFRMENTATION

	EQUIPMENT MAINTENANG	E TABLE-MIC	ROBIAL FERN	MENTATION	
	•				Labor
	Equipment Items	Cvcle Life	Unit Cost	\$/Cycle	Hours
		,,,,,,		<b>V. 0)01</b> 2	
	UF Waste Vessel				
/4É	Chromatography 1			<i>//////</i>	
, 10	Chromatography Column	///////	////////	/////	
	om omotography obtain	,	·		
	Pump				
	Inst.& Control System				
	Manifolding				
	Equilibration Vessel				
			7		• • 1
	Wash Vessel				(
	Eluent Vessel		-		
	Regenerate Vessel			·	1
	Storage Vessel				. 1
		[			
-	Waste Vessel(1)		,		
	Product Vessel	<u> </u>			
					1
*	Waste Vessel(2)				
17	Chromatography 2////				
	Chromatography Column		(////////	777777	//////
				i	. /
	Pump				. (
	Inst.& Control System				. \
	Manifolding				
	Equilibration Vessel				
	<u> </u>				/
	Wash Vessel				1
	Eluent Vessel				1
					/
	Regenerate Vessel			·	- 1

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

#### FIG. 640-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Shaf	ts									Lubric	ant		
		Mate	ria	ls						Labor		Materi	als		
	\$/Cycle	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item No	.Qty	Cycle	Lif
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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(As Amended)

FIG. 64P-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

EQUIFIENT MAINTENANCE TAB	T		L I LIBILIN	INITON
				Labor
Equipment Items	Unit	Cost	\$/Cycle	Hours
UF Waste Vessel				(
16 Chromatography 1////				
Chromatography Column				
Pump				
Inst.& Control System				
Manifolding	•			
Equilibration Vessel				
Wash Vessel	}			(
	ļ			<b>'</b>
Eluent Vessel			·	,
Regenerate Vessel				/
Storage Vessel				_ \
Waste Vessel(1)				
Product Vessel				į
Waste Vessel(2)				(
17 Chromatography 2////	////	///		/////
Chromatography Column		~~~		1
Pump				/
Inst.& Control System				\
Mani folding				
Equilibration Vessel				,
Wash Vessel				
Eluent Vessel				\
Regenerate Vessel				

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For: Method for Scheduling Solution Preparation in
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(As Amended)

#### FIG. 64P-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

<b>—</b>	:	Thermal		ia			٠.			
		Materia						,	Labor	
	\$/Cycle	Item No.	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycl
$\mathbb{Z}$										
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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FIG. 64Q-1
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

EQUIPMENT MAI				DIAL				-
	Filters						· · · · ·	
	Materia	ls	<b>,</b>					Labor
Equipment Items	Item No.	Oty	Cycle l	Life	Unit	Cost	\$/Cycle	Hours
Storage Vessel		,						
Waste Vessel(1)								
Product Vessel								·
Waste Vessel(2)								
18 Buffer Exchange/////								
Pump Filter Holder Manifolding Instrumentation								
UF Flush Vessel								
UF Prime Vessel	<u> </u>							,
UF Filtrate Vessel								
UF Wash Vessel								
UF Diluent Vessel						•		
UF Regeneration Vessel		-						
UF Storage Vessel								
UF Waste Vessel								(
19 Chromatography 3  Chromatography Column								<u>/////</u>
Pump Inst.& Control System								(
Mani folding								\
Equilibration Vessel								. /

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For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 640-2

		EQUIP	TENT	MAINTENANC	E TABLE-MIC	ROBIAL F	ERMENTAT	ION		
$\mathbb{Z}$		Gaskets							Beari	ngs
<u> </u>		Materia	ls				Labor		Mater	ial
	\$/Cycle	Item No.	Oty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item	No.
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 64R-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

			BIAL FERMEN		
• .					Labor
Equipment Items	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
		<u> </u>	<u>.</u>		
Storage Vessel			: •		ı
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)			-		
18 Buffer Exchange					
Pump					
Filter Holder					{
Manifolding					,
Instrumentation					
UF Flush Vessel		:		-	/
UF Prime Vessel	•				1
UF Filtrate Vessel		,		_	
UF Wash Vessel					
UF Diluent Vessel			·		(
UF Regeneration Vessel					· .
UF Storage Vessel	•			-	1
UF Waste Vessel		·			(
19 Chromatography 3////					
Chromatography Column					
Pump		İ			/
Inst.& Control System					(
Manifolding	l				)
Equilibration Vessel	- 1		1		

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For: Method for Scheduling Solution Preparation in
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(As Amended)

#### FIG. 64R-2 EQUIPMENT MAINTENANCE TABLE-MICRORIAL FERMENTATION

		Seal	S						· ·		Belts		
		Mate	rial	ls					Labor		Mate	ria	ŀs
	\$/Cycle	Item	No.	aty	Cycle Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No.	0t
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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### FIG. 64S-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

EQUIPMENT MAINTENAN	CE TABLE-NIC	CROBIAL FERI	ENTATION	
		-		Labor
Equipment Items	Cycle Life	Unit Cost	\$/Cycle	Hours
Storage Vessel	1			. (
Waste Vessel(1)				)
Product Vessel	1			
Waste Vessel(2)				. \
18 Buffer Exchange				
Pump			,,,,,,,	<del>ma</del>
Filter Holder				(
Manifolding				/
Instrumentation				}
UF Flush Vessel				/
UF Prime Vessel				\
UF Filtrate Vessel				)
UF Wash Vessel	·	٠		
UF Diluent Vessel		·		{
UF Regeneration Vessel	1			)
UF Storage Vessel				[
UF Waste Vessel	·			(
19 Chromatography 3////				
Chromatography Column				
Punp		]		/
Inst.& Control System				(
Manifolding			1	}
Equilibration Vessel				/
	1		ı	/

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 64S-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Shaf	ts									Lubri	cant		
_		Mate	ria	ls					<del></del>	Labor	··· · ·	Mater:	ials	· ·	
	\$/Cycle	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item N	o.Oty	Cycle	Life
										-					
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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FIG. 64T-1

EQUIPMENT MAINTENANCE TAB	LE-MICROBIA	L FERMEN	TATION
			Labor
Equipment Items	Unit Cost	\$/Cycle	Hours
Stange Vessel	! 	:	(
Storage Vessel			\
Waste Vessel(1)			
Product Vessel	·		(
Waste Vessel(2)			\
18 Buffer Exchange			
Pump			1
Filter Holder	]		(
Mani folding			1
Instrumentation			)
UF Flush Vessel			. /
UF Prime Vessel			
UF Filtrate Vessel			}
UF Wash Vessel			
UF Diluent Vessel			\
UF Regeneration Vessel			}
UF Storage Vessel		·	
UF Waste Vessel			(
19 Chromatography 3////			
Chromatography Column			
Pump	·		/
Inst.& Control System			
Manifolding			}
Equilibration Vessel			/-

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
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#### FIG. 64T-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Cycle	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle
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			1							
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

# FIG. 64U-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Filters	;				
	Materia	ls		·		Labor
Equipment Items	Item No	Oty	Cycle Life	Unit Cost	\$/Cycle	Hours
Wash Vessel	<u> </u>					
Eluent Vessel						
Regenerate Vessel			•			
Storage Vessel	1				·	
Waste Vessel(1)	1					
Product Vessel			-			
Waste Vessel(2)						•
20 Buffer Exchange						
Pump Filter Holder	}	ľ		·		
Manifolding	†				1	
Instrumentation						
UF Flush Vessel	1.		<u> </u> 			
UF Prime Vessel		}				
UF Filtrate Vessel				:		
UF Wash Vessel						
UF Diluent Vessel						j
UF Regeneration Vessel	1					,
UF Storage Vessel	1			,		
UF Waste Vessel	1					/
21 Chromatography 4////						
Chromatography Column	·					,
Pump	1	j				/

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 64U-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Gask	ets							·		Beari	ings
		Mate	ria.	ls						Labor		Mater	ial
	\$/Cycle	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No.
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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## FIG. 64V-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	EQUIPMENT MAINTEN	I	INDLL	ITOHOL	DIAL I	LIBILA	ILVITON :	•
		<u> </u>			·			<u> </u>
						· .		Labor
	Equipment Items	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours
	Wash Vessel		<u>                                       </u>					
	Eluent Vessel							
	Regenerate Vessel							
	Storage Vessel						:	
-	Waste Vessel(1)	ľ						
	Product Vessel						,	
	Waste Vessel(2)							
20	Buffer Exchange							
_	Pump			1				
	Filter Holder Manifolding			- 1				(
	Instrumentation				-			
	UF Flush Vessel						,	
	UF Prime Vessel							
	UF Filtrate Vessel							
	UF Wash Vessel					. =		
	UF Diluent Vessel							. 1
	UF Regeneration Vessel				-			(
	UF Storage Vessel						Ì	
<del>-</del>	UF Waste Vessel				•	٠ .		/
21	Chromatography 4							
	Chromatography Column							/
	Pump							/

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(As Amended)

FIG. 64V-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Seal	S.		*	-						Belt	S	
		Mate	ria	ls				•		Labor		Mate	ria	ls
	\$/Cycle	Item	No.	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No.	Qt,
	:													
	•						·					<i>:</i>		
		///	///			////	////	////			/////	///	///	100
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For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 64W-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

EQUIPMENT MAINTENANC	E IADL	E-UTC	HODIA	_ renr	ENIAITON	<del></del> ,
		<del></del>	<u></u> , -			Labor
Equipment Items	Cycle	Life	Unit	Cost	\$/Cycle	Hours
Wash Vessel						
Eluent Vessel	i i				·	,
						•
Regenerate Vessel						
Storage Vessel						
Waste Vessel(1)						
Product Vessel						·
Waste Vessel(2)						(
20 Buffer Exchange						
Pump						
Filter Holder					·	l (
Manifolding	1				<b> </b>	1
Instrumentation						
UF Flush Vessel	}					
UF Prime Vessel						
UF Filtrate Vessel					1	
UF Wash Vessel						
UF Diluent Vessel					·	j
UF Regeneration Vessel						(
UF Storage Vessel						
UF Waste Vessel						
21 Chromatography 4/////		////	////	////		
Chromatography Column			<i>(111)</i>		<i>//////</i>	
Pump			:			

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For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 64W-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Shaf	ts									Lubricant				_
		Mate	ria	ls						Labor	<del></del>	Mate				
1	\$/Cvcle				Cycle	Life	Unit	Cost	\$/Cvcle		\$/Cycle				Cycle	Lif
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FOUTPMENT MAINTENANCE TARLE-MICRORIAL FERMENTATION

EQUIPMENT MAINTENANCE TAB	LE-MIC	HORIA	L FERMEN	TATION
*				
				Labor
Equipment Items	Unit	Cost	\$/Cycle	Hours
Edathment Tremo	0.1.2.0	-	#/ U) UIC	110010
Wash Vessel				
Eluent Vessel				}
Regenerate Vessel				
Storage Vessel				
Waste Vessel(1)				}
Product Vessel				
Waste Vessel(2)	·			(
20 Buffer Exchange				
Pump	7777		77777	any
Filter Holder	Ì			[
Manifolding				1
Instrumentation			·	1
UF Flush Vessel				0.0
UF Prime Vessel				1
UF Filtrate Vessel				1
UF Wash Vessel				/
UF Diluent Vessel				
UF Regeneration Vessel				\
UF Storage Vessel				$\rangle$
UF Waste Vessel				/
21 Chromatography 4////	////	7///	/////	
Chromatography Column		////		)
Pump	•			/

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

FIG. 64X-2
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

•		EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION  Thermal Media											
١			Ther	mal	Med	ia							
1	$\int_{-\infty}^{\infty}$		Mate	rial	s						Labor		
1		\$/Cvcle	Item	No.	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	
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For: Method for Scheduling Solution Preparation in
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### FIG. 64Y-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Filters							
	Materia	ls.	:					Labor
Equipment Items	Item No.	,	Cycle	Life	Unit	Cost	\$/Cycle	Hours
Inst.& Control System								
Manifolding Equilibration Vessel							•	
Wash Vessel		·						
Eluent Vessel					-			
Regenerate Vessel	1							
Storage Vessel							: •	. (
Waste Vessel(1)								
Product Vessel Waste Vessel(2)								(
22 Sterile Filtration		////	/////			////		
MF Wash Vessel		777					,,,,,,	
Pump Filter Holder							·	1
Manifolding Instrumentation	-							
MF Flush Vessel	1	,						ı
MF Prime Vessel	]						·	(
MF Filtrate Vessel							·	
MF Wash Vessel								/

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
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(As Amended)

## FIG. 64Y-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Gaskets				,			Bearing
		Materia	ls				Labor		Materia
	\$/Cycle	Item No.	Oty	Cycle Life	Unit Cost	\$/Cycle	Hours	\$/Cycle	Item No
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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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(As Amended)

### FIG. 64Z-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

					<del></del>	·	
			<del></del>	<del></del> -			Labor
Equipment Items	Qty	Cycle L	ife	Unit	Cost	\$/Cycle	Hours
Inst.& Control System			-		<u></u> :		· · · · · ·
Manifolding				•		·	
Equilibration Vessel							-
Wash Vessel						. ,	
Eluent Vessel							
Regenerate Vessel				•		·	
Storage Vessel							
Waste Vessel(1)	-	•		:	:		
Product Vessel							
Waste Vessel(2)		•					(
22 Sterile Filtration							
MF Wash Vessel					,,,,,		
Pump		•					
Filter Holder					•		
Manifolding			I				
Instrumentation			1				
MF Flush Vessel							
MF Prime Vessel							(
MF Filtrate Vessel							
MF Wash Vessel						·	

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### FIG. 64Z-2 FOUTPMENT MAINTENANCE TABLE-MICRORIAL FERMENTATION

		Seals								Belt	S	
		Materia	ls					Labor		Mate	ria	ls.
	\$/Cycle	Item No	Oty	Cycle Lif	e Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No.	Qt
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For: Method for Scheduling Solution Preparation in
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## FIG. 64AA-1 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

· · · · · · · · · · · · · · · · · · ·	1		<del></del>			· · · · · · · · · · · · · · · · · · ·
						1 -1 -
				•		Labor
Equipment Items	Cycle	Life	Unit	Cost	\$/Cycle	Hours
Inst.& Control System			-	<u>_</u> -		
Manifolding	Į					
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel (1)						
Product Vessel						
Waste Vessel(2)		ļ				
22 Sterile Filtration///			////	////		
MF Wash Vessel		///		////	/////	/////
Dumo						
Pump Filter Holder		į				,
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						· (
MF Filtrate Vessel				:		
MF Wash Vessel						

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600

For: Method for Scheduling Solution Preparation in
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(As Amended)

### FIG. 64AA-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

7	_	Shafts Lubricant															
١	_		Shaf	ts									Lubr	ica	nt		
1	/		Mate	rial	s	-					Labor		Mate	ria	s		
		\$/Cycle	Item	No.	Oty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle	Item	No.	Qty	Cycle	Life
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(As Amended)

FIG. 64AB-1 FOUTPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

EQUIPMENT MAINTENANCE TAB	FE-MICHODIA	IL FERMEN	IAITUN
			Labor
Equipment Items	Unit Cost	\$/Cycle	Hours
Took C Cookeel System			
Inst.& Control System			(
Manifolding			· )
Equilibration Vessel			
Wash Vessel			(
Eluent Vessel			• •
Regenerate Vessel			/
Storage Vessel			
Waste Vessel(1)			\
Product Vessel			
Waste Vessel(2)	·		\
22 Sterile Filtration			
MF Wash Vessel			
Pump		e	
Filter Holder	]		. {
Manifolding	}		\
Instrumentation	·	**	)
MF Flush Vessel			
MF Prime Vessel	·		. (
MF Filtrate Vessel			\
MF Wash Vessel			

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FIG. 64AB-2 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

<u> </u>		Ther	mal	Mod	lia			· · · ·		<u> </u>	
<b>}</b> -		Mate								Labor	
	\$/Cycle	Item	No.	Qty	Cycle	Life	Unit	Cost	\$/Cycle	Hours	\$/Cycle
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#### FIG. 65A-1 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

		MASTER PROCESS PARAMET			<del>/</del>
			Group 1	<u> </u>	
	Unit Operation Type	Parameter	Soln.		Parameter
T1	Inoculum Prep	Number of Flasks Media Volume/Flask		0.25 Liters	Temperature Agitation Duration
15	Flask Growth	Scale Up Ratio Media Volume/Flask	·	10 Fold 1.25 L	Temperature Agitation Duration
13	Fermentation Production	Scale Up Ratio Fermentor Working Volume Antiform A Antiform B Base Acid	S-101 S-102 S-103 S-104 S-105	10 Fold 500 Liters 1 MI/L 1 MI/L 5 MI/L 5 MI/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
T4	Initial Seeding	Number of Ampules Volume Per Ampule Starting Cell Density Ampule Solit Ratio Culture Vessel Type Feed Volume		2 2 MI 300.000 Cells/MI 1 Vessels/Ampule Roll. Bot. 100 MI	Serum Content Feed Rate Days to Confluence
15	Culture Vessel Split	Vessel Split Ratio New Vessel Type Feed Volume Serum Content		2 R8 100 MI 2.0% Fetal Bovine Serum	Feed Rate Days to Confluence
16	Spinner Flask Seeding	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Hedia Washes No.of Media/Serum Washes		4 Liters 0.1 L Cerls/L Flask 5 Ga/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
17	Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No.of Media/Serum Washes		500 Liters 8.3 5 Ga/Liter 2 1	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
18	Biosynthesis Bioreactor Preparation (Hollow Fiber Reactor)	Reactor Feed Volume Number of PBS Washes Number of Media Washes No. of Media/Serum Washes Serum Content		100 Liters 2 2 2 2 2.0% Fetal Bovine Serun	Number of Reactors Feed Rate Days to Confluence
79	Bioréactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume uCarrier Density Number of PBS Washes Number of Hedia Washes No. of Media/Serum Washes Serum Content		Liters Gas/L	Number of Reactors Feed Rate Days to Confluence
10	Initial seeding	Number of Annules Volume Per Annule Starting Cell Density Annule Split Ratio		2 2 MI 300,000 Cells/MI 1 Vessels/Ampule	Serum Content Feed Rate Days to Confluence

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For: Method for Scheduling Solution Preparation in
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(As Amended)

### FIG. 65A-2 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

	Group 2		·	Group 3	
_	Soln.		Parameter	Soln.	
•		37 C 200 RPM 18 Hours	Final 00		12
		37 C 200 Hours 18 RPM	Final OD		12
	·	37 Hours 1 HP/100L 1.5 VVM 5 PSIG 21 Hrs	Final OD Dry Cell Mass Product Concentration CIP		9.96 Gas TDCM/L 0.3 Gas Product/L Y
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concen.	/	2500% Mg Prod/L 0.125 Mg TP/MI
	·	1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concen.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%

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(As Amended)

## FIG. 65B-1 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

	٠		<b>Group</b>	1	
	Unit Operation Type	Parameter	Soln.		Parameter
		Culture Vessel Type Feed Volume	-	Roll. Bot. 100 MI	PBS Washes Trypsin Wash
11	Culture Vessel Split	Vessel Split Ratio New Vessel Type Feed Volume Serum Content		RB 2 100 MI 2.0% Fetal Bovine Serum	Feed Rate Days to Confluence PBS Washes Trypsin Wash
12	Spinner Flask Split	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		4 Liters 0.1 L Cells/L Flask 5 Ga/Liter 2 1 2	Serum Content Feed Rate Days to Confluence
13	Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		500 Liters 8.3 5 Gm/Liter 2 1	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
	Bioréactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume uCarrier Density Number of PBS Washes No. of Media/Serum Washes Serum Content		Liters Gas/L	Number of Reactors Feed Rate Days to Confluence
		Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		4 Liters 0.1 L Cells/L Flask 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
16		Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		500 Liters 8.3 5 Ga/Liter 2 1 2	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
ולו	Pentide Cleavage	Reactor Feed Volume Number of PBS Washes Number of Hedia Washes No. of Hedia/Serum Washes Serum Content		100 Liters 2 2 2 2 2 2.0% Fetal Bovine Serun	Number of Reactors Feed Rate Days to Confluence
18	Tissue Thawing	Crude Product Yield Environmental Temperature Thaw Duration		25 Gm Crude Prod./Kg Tissue 25 C 16 Hours	Contaminant Protein Con
191		Crude Product Yield Liquid/Solid Ratio Hommogenization Temp Hommogenizer Type Energy Input Duration		25 Go Crude Prod./Kg Tissue 10 L Solution/Kg Tissue 4 C RS 200 HP/100L/Hr 4 Hours	Contaminant Protein Com
q١	iquid Thaving			7 71001 0	

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## FIG. 65B-2

### MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

	Group 2			Group 3	
	Soln.		Parameter	Soln.	
1		200 HI 100 HI			
		1 Feed per vessel per 2 Days 2 Days 200 HI 100 HI	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concen.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
		100 Gm/L	Temperature Regulation CIP SIP	, i	
		100 Ga/L	Temperature Regulation CIP SIP	Y	
+	- +		Amplification Factor		100%

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## FIG. 65C-1 NASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Ţ	MASTER PROCESS PARA			
Unit Operation Type	Parameter	Soln.		Parameter
			,	
Product Ppt by Solids	Reagent Concentration		1 H	Kgms of Reagent/Liters Prod Temperature Addition Time Additional Mix Time
2Product Ppt by Liquids	Reagent Concentration		1 H	Liters Reagent/Liters Produ Temperature Addition Time Additional Mix Time
Contaminant Ppt by Solids	Reagent Concentration		1 H	Kgms of Reagent/Liters Prod Temperature Addition Time Additional Mix Time
Contaminant Ppt by Liquid	is Reagent Concentration		1 H	Liters Reagent/Liters Produ Temperature Addition Time Additional Mix Time
Solids Harvest Tangential Flow MF	Porosity Average Flux Rate Total Throughput Filtration Time		0.2 Micron 11 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 1 HR	Flush Prime Concentration Factor Wash Regenerate Store
Continuous Centrifugation Solids Harvest	n System Void Volume		5 Liters	RCF Time Volume Reduction Wash Volume
Continuous Centrifugation Supematant Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
Dilution	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
Batch Centrifugation Solids Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume

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(As Amended)

FIG. 65C-2

#### MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2	? ·		Group :	3
Soln.		Parameter	Soln.	
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \				
	0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y
	0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y
	0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y
	0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y
	2 L/SF 2 L/SF 10 Fold 0.5 L/SF 1 L/SF 2 L/SF	Step Recovery of Product Step Recovery of I.P. Temperature Regulation CIP SIP		95% 95% Y
	10,000 X 6 50 Minutes 30 X Vol. Reduction 0.2 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y
	10,000 X G 30 Minutes 0.062 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		85% 0.3 Y
	10,000 X 6 . 30 Minutes 16 X Vol. Reduction 1.5 X System Vold Volume	Step Recovery of Product Step Recovery of T.P.		95% 0.95 Y
	10,000 X 6 30 Minutes 16 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P.		95% 0.95 Y

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## FIG. 65D-1 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

			Group 1		
Unit Ope	ration Type	Parameter	Soln.		Parameter
30 Batch Ce Supenate	ntrifugation nt Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
31 Cell Dis High Pre	ruption ss. Homogen.	Product Temperature Utility Temperature Void Volume		8 C 2 C 5 Liter	Number of Passes Pressure Flow Rate Temperature Increase
32 Cell Dis Bead Mil	ruption 1	Number of Passes Bead Size Yold Volume Flow Rate		0.5 LPN	
Cell Dis Chemical	ruption Lysis	Reagent Temperature Exposure Time		0.5 M NaOH 4 C 2 Hours	Liters Reagent/6n Produc Titration
34 Microfil Tangenti	tration al Flow	Porosity Average Flux Rate Total Throughput		0.2 Micron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF	Flush Prime Wash Solids Regenerate
35 Microfil Dead End		Filtration Time Porosity Average Flux Rate Total Throughput Filtration Time		2 HR 0.2 Kicron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 0.5 HR	Störe Flush Prime Wash Solids Regenerate Store
16 Ultrafil Concentra	tration ation/Dilution	Porosity Average Flux Rate Concentration Time		6.5 K NIML 3 L/SF/HR at 40 Psig at 4 C 2 HR	Store Flush Prime Wash Dilute Concentrate Solids Regenerate
37 Ultrafil Flow Dia		Porosity Average Flux Rate Dialysis Ti <b>n</b> e		60 K NM/L 3 L/SF/HR at 40 Psig at 4 C 2 HR	Flush Prime Dialysis Buffer Wash Solids Regenerate
BProd.Ads HPLC	.Chromatography	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity	1	O MG Prod./MI Of Packing 1.5 Fold 0.37 H/O 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
Prod.Ads	.Chronatography	Column Capacity Column Oversize Factor	1	O MG Prod./MI Of Packing 1.5 Fold	Column Equilibration Column Wash

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For: Method for Scheduling Solution Preparation in
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(As Amended)

#### FIG. 65D-2

#### MASTER PROCESS PARAMETERS TABLE-BLOPHARMACELITICAL

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL							
Group	2		Group 3				
Soln.		Parameter	Soln.				
	ļ	SIP		Y			
	10,000 XG	<del></del>		<u> </u>			
	30 Minutes 16 X Vol. Reduction	Step Recovery of Product Step Recovery of T.P.		95% 0.95			
	1.5 X System Void Volume	Temperature Regulation CIP SIP		Y Y Y			
	6 Times 12,000 PSI 5 LPM 1.8 Degrees C/1,000 PSI	Rinse Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP		500% Void Volumes 95% 95% Y Y Y			
		STP Step Recovery of Product Step Recovery of T.P.		95%			
	·	Temperature Regulation CIP SIP		Y			
	0.4 L/Gm 0 MI/Liter	Step Recovery of Product Step Recovery of T.P.		95%			
		Temperature Regulation CIP SIP		Y			
	2.00 L/SF 2.00 L/SF 0.50 L/SF	Step Recovery of Product Step Recovery of T.P.		95% 95%			
	0.30% Of Product Solution 1.00 L/SF 2.00 L/SF	Temperature Regulation CIP SIP		Y Y			
	0 L/SF 0 L/SF 0.50 L/SF	Step Recovery of Product Step Recovery of T.P.		95% 0.95%			
	0.003 Of Product Solution 1 L/SF 2 L/SF	Temperature Regulation CIP SIP		N N N			
	2.00 L/SF 2.00 L/SF 0.50 L/SF 10.0 Fold 0.30% Of Product Solution	Store Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP	8	2.00 L/SF 95% 95% Y Y			
	1.00 L/SF 2 L/SF 2.00 L/SF	SIP Store Step Recovery of Product		200% L/SF			
	5.0 X Feed Stream Volume 0.50 L/SF 0.30% Of Product Solution 1.00 L/SF	Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y			
	5 Column Volumes 3 Column Volumes 3 Column Volumes 0 Column Volumes 1 Column Volumes 2 Column Volumes	Prod.Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		80% 95% 95% N			
	5 Column Volumes 3 Column Volumes	Prod.Elution Volume Step Recovery of Product		Y 80% 95%			

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Dkt No.: 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

## FIG. 65E-1 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

<del>- } - : - : - : </del>	MASTER PHUCESS PARAME	IENS IADI	E-DEUTHANNACEUTICAL	
	·			
Unit Operation Type	Parameter	Soln.		Parameter
	Column Aspect Ratio Max. Linear Velocity		0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Elute A Column Elute B Column Regenerate Column Store
40 Prod. Ads . Chromatography LPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Prod./M1 Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
11 Cont .Ads .Chromatography HPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		30 MG Cont./M1 Of Packing 1.5 Fold 0.37 H/O 100 Co./Hr at 45 Psig and 4 C	Column Wash Column Elute A Column Elute B Column Regenerate Column Store
12 Cont .Ads .Chromatography MPLC	Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 HG Cont./H1 Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 400% C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
13 Cont .Ads .Chromatography LPLC	Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Cont./Ml Of Packing 1.5 Fold 0.37 M/D 100 Cm/Hr at 45 Psig and 4 C	Column Wash Column Elute A Column Elute B Column Regenerate Column Store
44Size Excl .Chronatography HPLC	Load Capacity Length Max. Linear Velocity Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
45 Size Excl.Chromatography HPLC			5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
46 Size Excl.Chromatography LPLC	Load Capacity Length Hax. Linear Velocity  Yoid Volume		5% of Total Column Volume 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
17 Dilution	Dilution Factor		3 Liters/Liter	Dilution Time Additional Mix Time (
48 Resolubilization	Reagent/Product Ratio		0 L/Kg Product	Reagent 1 Concentration
1.	Dissolution Time Additional Mix Time		0.50 Hours 0.50 Hours	. '

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(As Amended)

FIG. 65E-2
MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

	MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL							
Group	<u> </u>		Group 3	<u>;</u>				
Soln.		Parameter	Soln.					
	3 Column Volumes 0 Column Volumes 1 Column Volumes 2 Column Volumes	Step Recovery of T.P. Temperature Regulation CIP SIP	·	95% N Y Y				
	5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% 95% 95% 95% Y				
	5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% 95% 95% 95% Y				
	5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes 2 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of I.P. Temperature Regulation CIP SIP		42% 95% 95% 95% Y				
)	5 Column Yolumes 3 Column Yolumes 3 Column Yolumes 2 Column Yolumes 1 Column Yolumes 2 Column Yolumes	Prod. Elution Volume Step Recovery of Product Step Recovery of I.P. Temperature Regulation CIP SIP		42% Columns Volumes 95% 95% 95% N Y				
	4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% Columns Volumes 95% 95% N Y				
	4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% Columns Volumes 95% 95% N Y				
	4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% Columns Volumes 95% 95% N Y Y				
	0.5 Hours 1 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y				
	Water Dist.	Step Recovery of Product Step Recovery of T.P.		95% 95%				
\	,	Temperature Regulation CIP SIP		Y				

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(As Amended)

### FIG. 65F-1 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

MASIEM PHOLESS PARAMEICHS INDIE-DUUTHANNACCUITUAL								
			Group	1				
	Unit Operation Type	Parameter	Soln.		Parameter			
49	Enzymatic Modification	Enzyme to Product Ratio Enzyme Concentration Reaction Temp. Reaction Duration		0.084 Liters of Enzyme Stock Per Liter of Start Proc. Vol. 2 Mg/MI 37 Degrees C 30 Minutes 100%	Titration Solution-1 Titration Solution-2 Neutralization			
50	Lyophilization	Product Capacity/Load Product Unit Size		8 Units 100 Grams/Unit	Lyophilization Time Product Weight Reduction			
51	Heat Exchange	Process Initial Temp. Process Final Temp Utility Initial Temp. Utility Final Temp. Process Specific Heat Design Type(P.T.C)		98.6 Degrees C 39.2 Degrees C 34 Degree C 5 Degrees C 38.6 K BTU/Hr	Exposure Time			
52	Storage		,					
53	Fermentation Seed	Scale Up Ratio Fermentor Working Volume Antifoam A Antifoam B Base Acid		10 Fold 50 Liters 1 MI/L 1 MI/L 5 MI/L 5 MI/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration			
54	Initial Seeding	Flask Feed Volume Spinner Split Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serun Washes	·	12 Liters 4 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence			
55		Flask Feed Volume Spinner Split Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		12 Liters 4 5 Ga/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence			
56	Culture Flask Split	NO. OF THEOLOGICAL MICHIES		£ 100				
57	Stirred Tank Reactor							
58	Fluidized Bed Reactor	Process Initial Temp. Process Final Temp Utility Initial Temp		37 Degree C 4 Degree C 2 Degree C	Exposure Time			

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(As Amended)

## FIG. 65F-2 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

		MASTER PROCES	s parameters table-blopharma	ICEUITCA	L ,
	Group 2		·	Group 3	3
ot	Soln.		Parameter	Soln.	
		0.067 L/L Process 0.02 L/L Process 0.57 L/L Process	Step Recovery of Product Step Recovery of T.P.		95% 95%
		0.J/ E/E FIDLESS	Temperature Regulation CIP SIP		Y Y Y
		18 Hours 0.95	Step Recovery of Product Step Recovery of T.P.		95% 95%
			CIP SIP		Y
		1 Hours	Step Recovery of Product Step Recovery of T.P.		100% 100%
			Temperature Regulation CIP SIP		Y Y
}			Step Recovery of Product Step Recovery of T.P. Temperature Regulation	<u> </u>	95% 95% Y
		37 Hours	CIP		Ý 12
		1 HP/100L 1.5 YVH 5 PSIG 21 Hrs	Final OD CIP		Y
	·	2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		i
		2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		1
			Step Recovery of Product Step Recovery of T.P.		0.95 95%
			CIP SIP		Y Y Y
		50% Hours	Step Recovery of Product Step Recovery of T.P.		0.95 100%

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# FIG. 65G-1 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

			Group 1		
	Unit Operation Type	Parameter	Soln.		Parameter
		Utility Final Temp. Process Specific Heat Design Type(P.T.C)		5 Degrees C 12 K BTV/Hr P	:
9	Liquid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Addition Duration Additional Mix Duration Mix Energy		1 L Extraction/L Product 4 C 0.5 Hours 4 Hours 0.3 HP/100 L	Phase Separation Time Product Phase(Top/Botto Harvest Time
0	Solid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Duration Hix Energy		1 L Extraction/L Product 4 C 4 Hours 0.3 HP/100 L	Phase Separation Time Product Phase(Top/Botto Harvest Time

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FIG. 65G-2 MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

$\Box$	Group 2			Group 3	3
	Soln.		Parameter	Soln.	
$\langle \ \rangle$			Temperature Regulation CIP SIP		Y Y Y
<del>/ -</del>		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		0.9 50% Y
/ \		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		0.9 50%